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VOL. 70 NOVEMBER, 1955 NO. 5

Original Communications

THE OBSERVED EMBRYOLOGY OF HUMAN SINGLE-OVUM TWINS AND OTHER MULTIPLE BIRTHS*

GEORGE W. CORNER, M.D., SC.D., BALTIMORE, MD.

(From the Department of Embryology, Carnegie Institution of Washington)

LONG ago it was noticed that in some cases of human twinning the two individuals resemble each other very closely, whereas in other cases they differ in features and in coloring, and may be of different sex. From about 1866 to 1880, several physicians and biologists in different countries independently developed the concept that the "identical" twins come from a single fertilized egg and the nonidentical or fraternal twins from two separate eggs.[1] Three circumstances obviously support this conjecture, and account for the ready way in which it has been accepted as a working hypothesis by physicians, biologists, and laymen, in spite of the slowness of the embryologists to confirm it by actual specimens of early embryos in which the process of duplication can be seen. The first circumstantial evidence is that single-ovum twinning has been seen in the developing eggs of fishes and birds. The second has long been available; this is the observation by physicians and midwives that some pairs of twin babies have only a single placenta and are enclosed, before birth, in a common, single chorioamniotic membrane. From what we know about the embryology of the membranes, the presence of two embryos in one chorion is most easily explained by assuming that they originated from a single egg cell. The third kind of circumstantial evidence is that given us by the young science of genetics. From the standpoint of inheritance theory, if two individuals born at the same time are exactly alike,

*The Annual Joseph L. Baer Lecture of the Chicago Gynecological Society, delivered Oct. 15, 1954.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

they must have an identical genic composition such as would exist if they both got all their genes from one and the same egg fertilized by one single spermatozoon. This explanation of identical twinning is so satisfactory that it has been taken up by the popular literature of human genetics as if it were a proved and fully understood fact.

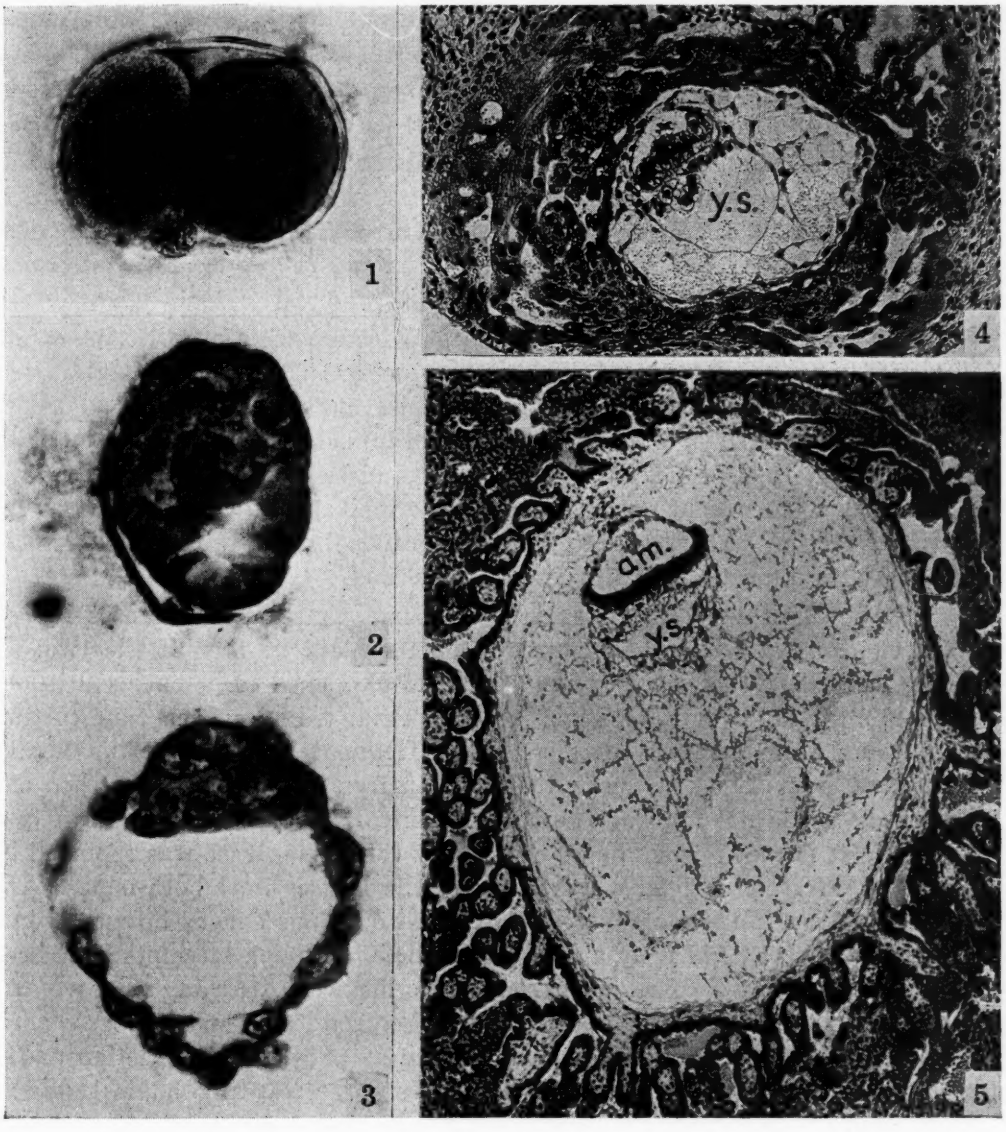
Meanwhile the embryologists and the obstetricians have built up on paper the morphological theory of single-ovum twinning, tracing the various ways in which one egg cell might ultimately develop into two embryos. All this is in the textbooks; it has chiefly been worked out by deduction from the arrangement of the placentas and fetal membranes as seen at birth or in fetal life. Embryonic specimens early enough to provide direct corroboration of the theory are rare. The purpose of the present lecture is to review the embryological theory; to consider how far it is actually supported by observation of twin embryos and by relevant experiments on animals; and, above all, to present illustrative early cases from the Carnegie collection of human embryos and from other sources which have generously been placed at my disposal.

I. Separation of the Early Blastomeres

Figs. 1 to 5, with their legends, will serve to provide the necessary background of early human embryology for our subsequent analysis of twinning. There are three critical stages at which twinning might occur. The earliest of these is the stage, illustrated in Fig. 1, when the fertilized egg cell has divided into two daughter cells or blastomeres. Separation of the two cells at this time might give rise to two embryos instead of one. This possibility has frequently been suggested and on the other hand has been doubted by experienced biologists. In considering it we are confronted by one of the fundamental questions of development, that of the potentiality for development possessed by the elements of a developing organism. The fertilized egg ultimately differentiates into all the kinds of cells that make up the adult body; the adult cells, however, can produce only their own or closely related kinds of cells. Somewhere in the course of their multiplication the embryonic cells lose the totipotentiality that is characteristic of the egg. This loss may begin almost at once. In some of the invertebrates and lower vertebrates with which experiments can easily be done, it is known that once the egg has divided into two cells, the individual daughter cells can no longer produce a whole embryo. In many other species, however, the first two blastomeres are still totipotent, and each can grow into a normal full-sized embryo. This may be true even at a later stage, when the egg has divided into a many-celled mass, fragments of which will still form whole embryos. The reasons for these differences are technical and need not be reviewed here.

We have no information at all, of any direct kind, about the potentiality of the early human blastomeres, and almost none about any other mammal. J. S. Nicholas and his co-worker, B. V. Hall,[2] experimenting on rats, succeeded in a few cases in separating the first two blastomeres by dissection with a needle or a fine jet of water. When returned to the uterus, these cells each developed into normal-looking embryos. A very few of these lived in utero

as long as nine days. That they did not survive to term (21 days) is not surprising in view of the drastic treatment they had unavoidably received. Another experimenter had more spectacular success with a somewhat simpler undertaking. Seidel[3] removed rabbit embryos from the oviduct at the two-



Figs. 1-5.—Five stages of early human development illustrating the various phases at which twinning may occur.

Fig. 1.—Two-cell stage, from oviduct about day 2 after ovulation (No. 8698). (×300.)

Fig. 2.—Morula from uterine cavity about day 4 (No. 8794). Segmentation cavity is forming and inner cell mass begins to be differentiated. (×350.)

Fig. 3.—Blastocyst from uterine cavity, about day 5 (No. 8663). Well-defined inner cell mass. (×500.)

Fig. 4.—Implanted embryo, previllous stage, about day 11 (No. 7699). Germ disc has a small amniotic cavity above it and yolk sac (*y.s.*) below. (×100.)

Fig. 5.—Embryo of about day 17 (No. 7802). Under higher magnification the primitive streak can be recognized in the germ disc. (×50.)

(From Contrib. Embryol., Carnegie Inst., Washington, by courtesy of A. T. Hertig, John Rock, and C. H. Heuser.)

cell stage and punctured one of the blastomeres with a fine glass needle inserted through the zona pellucida. When the ovum was returned to the uterus of a foster mother, the other, unharmed blastomere continued its development. In two of 27 trials the young rabbit went on to birth at term. In the present year Brochart[4] reported attempts to separate the rabbit's blastomeres by an ingenious but rather rough mechanical trick. One of his experiments resulted in development and implantation of an embryo derived from a blastomere of the two-cell stage; this, however, died in utero after day 13 of gestation.

That is all the evidence we now have about the potentiality of the early blastomeres in mammals. It allows us at least to suppose that in man, as in the rat and rabbit, the first two blastomeres are totipotent, and to that extent supports the hypothesis that single-ovum twinning may arise from their separation.

Two embryos which originated thus would start their intrauterine career just as if they were a pair of double-ovum twins. They would progress separately through the tube and would become implanted separately. Each would develop its own placenta and membranes. At birth the obstetrician would have no means of knowing that they had come from a single egg cell. If through some mischance an opportunity to inspect the ovaries occurred during gestation, the fact that only one corpus luteum was present would suggest, but not prove, that only one egg was shed.

I say not prove, because exactly the same picture—two fetuses in separate chorions and only one corpus luteum—would be seen if the two offspring were derived from two eggs that had happened to be enclosed in one ovarian follicle. Every histologist sees bi-ovular follicles from time to time in sections of mammalian ovaries. How frequent they are in the human ovary, and how often they grow to full maturity and their eggs are shed and fertilized, we do not know. There is reason to think that ovulation of two-egg follicles is rare. One almost completely convincing case was reported by Wieman and Weichert,[5] in which however the fetuses were both males. The presence of two fetuses of opposite sex, with only one corpus luteum, would strongly suggest origin from a bi-ovular follicle, although attempts have been made to explain such cases theoretically in other ways. At any rate, we cannot rule out this possibility, and therefore the production of twins by separation of the blastomeres can never be absolutely proved by inspection of the products of conception. Unless an age arrives of "test-tube babies" and of experimental embryology on human beings like that done by Nicholas, Seidel, and Brochart on rats and rabbits, this type of human twinning must remain a plausible conjecture.

Genetic and obstetrical evidence, however, definitely favors it, for there are many cases in which twins of the identical variety are known to have been enclosed in separate chorions, with separate placentas. The history of this part of the problem is fully told by Price.[6] Stating the situation in technical terms, the proportionate number of genetically monozygotic twins is considerably larger than that reported by the obstetricians as monochorial. The

theoretical explanation of this difference seems to have been first offered by the American anatomist-geneticist C. H. Danforth,[7] who suggested that the discrepancy represents the number of cases in which uniovular twins develop in separate sets of fetal membranes. Such development can be explained only by the supposition that the two individuals with presumably identical gene patterns started as a single fertilized ovum which gave rise to two embryos before implantation. Essen-Möller[8] found that among 190 pairs of identical twins collected by himself and previous writers, 63, or 33 per cent, were dichorial. Vermelin and Ribon,[9] with an almost equally large collection of cases, approached the question in a slightly different way by an arithmetical analysis based on distribution of sex within the pairs. Among 500 cases of twin births in the Maternité of Nancy there were 385 dichorial pairs, of which 227 were of the same sex and only 158 bisexual. If these had all been of the double-ovum variety, the numbers of same-sex and opposite-sex pairs would have been approximately equal. The discrepancy is explained by assuming that the excess (69) represents cases of twinning by separation of the early blastomeres. Adding to this figure the number (109) of monochorial twins in the series, we get 178 single-ovum pairs, of which 38 per cent (i.e., the 69 excess dichorials) are assumed to have been produced by blastomere separation. This is only a little higher than Essen-Möller's figure. The proportion of single-ovum twins of all types in the whole group, thus estimated, is 178 of 500 cases, or 36 per cent, and like Essen-Möller's figure of 33 per cent is higher than that usually arrived at on the basis of the membranes.[10 11] Regardless of arithmetical detail, however, these two genetico-obstetrical investigations agree in pointing to blastomere separation as the method of embryonic duplication in about one-third of all cases of single-ovum twinning.

II. Duplication of the Inner-Cell Mass

The second phase of development at which twinning may occur is that illustrated in Fig. 3. The embryos of all mammals pass through a stage in which the rapidly dividing cells produce at first a solid ball-like mass or morula. Among these cells a few which are destined to become the active embryo are surrounded by others which will give rise to the membranes. When the segmentation cavity develops within the morula, the clump of embryo-forming cells (inner cell mass) is left at one pole of the hollow blastocyst (Fig. 3).

In human development the inner cell mass is recognizable about day 4 after ovulation; implantation occurs about day 7. If during this period some accident of development causes division of the inner cell mass, or starts the growth of two inner cell masses, then we have the beginning of twin embryos that will be enclosed in a single chorion.

Fig. 6, *A* shows hypothetically the earliest stage of this kind of twinning as it would appear about day 5. It has actually been seen (in another species) at a stage only a little later. Richard Assheton,[12] an excellent nineteenth century English embryologist, saw a blastocyst of the sheep, only about 7 days old, in which there were two inner cell masses. Unfortunately he published

only a crude sketch of his specimen, which remains to this day the earliest known mammalian single-ovum twin; but his description is clear, and Fig. 6, *B*, an artist's rendering of his diagram, gives a good idea of what it was like in section. G. L. Streeter[13] found a blastocyst of the pig about 13 days old which had two embryonic areas. A cross section of this blastocyst is accurately drawn in Fig. 6, *C*. The yolk sac develops early in the pig, and therefore there is only one yolk sac for the two embryos.

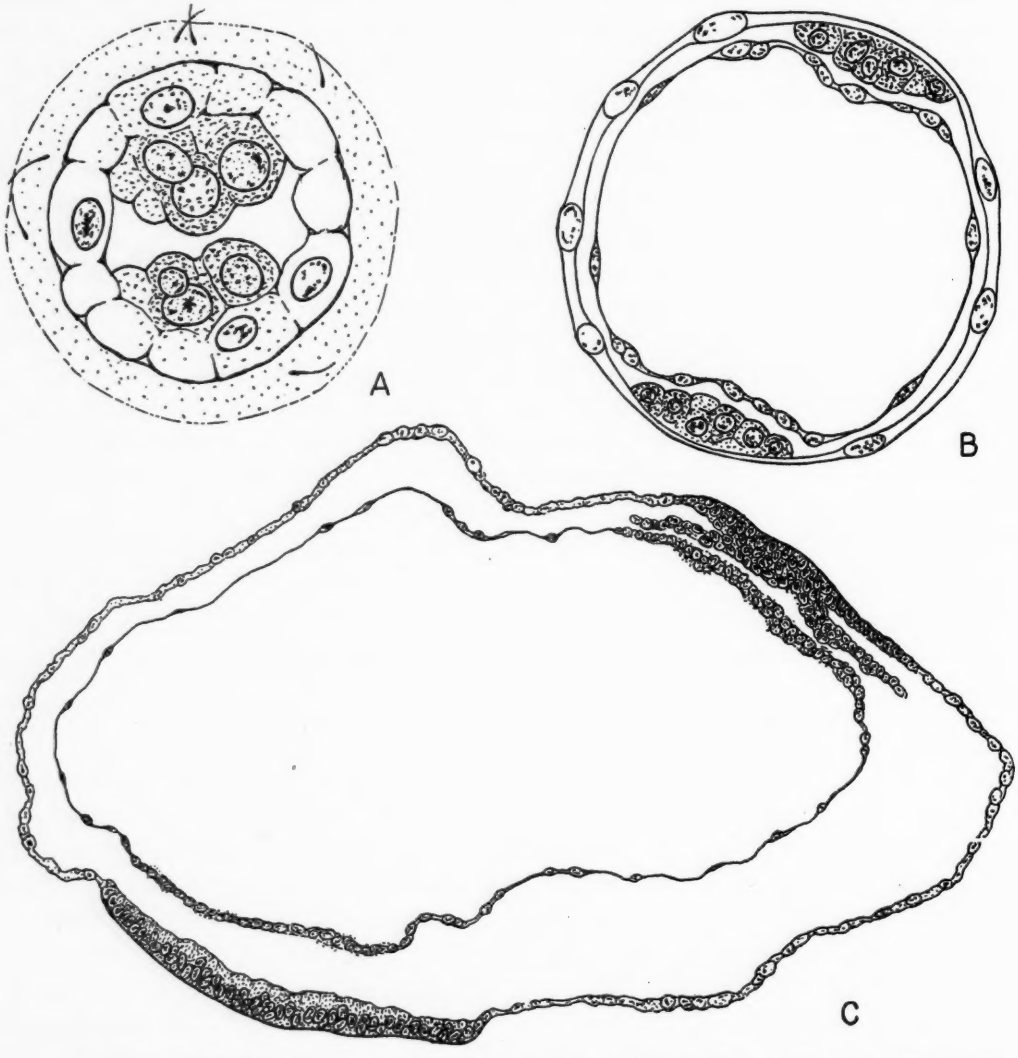


Fig. 6.—*A*, Hypothetical early stage of twinning by formation of two inner cell masses. *B*, Assheton's 7-day twin blastocyst of sheep. *C*, Streeter's twin blastocyst of pig of about 13 days. (Redrawn from original of Fig. 5, G. L. Streeter, Am. J. Anat. 34: 189, 1934.)

When such a pair of twins occurs in the human species, the subsequent development will follow the pattern shown diagrammatically in Fig. 7, *A* to *C*. Each of the two embryonic areas will reach, about day 16 or 17, the condition shown in Fig. 7, *C*.

A pair of human twins at this stage was discovered in 1952 by Dr. Chester H. Heuser in a human uterus removed at operation, that was given to him by Dr. Edgar A. Pund, Professor of Pathology at the University of Georgia. This is at present the earliest known human twin embryo.* It was described briefly by Dr. Heuser[14] (1954) and has been deposited in the Carnegie collection (No. 9009). In this specimen a single chorion contains twin embryos, each of which has its own amnion and yolk sac. They are about 17 days old

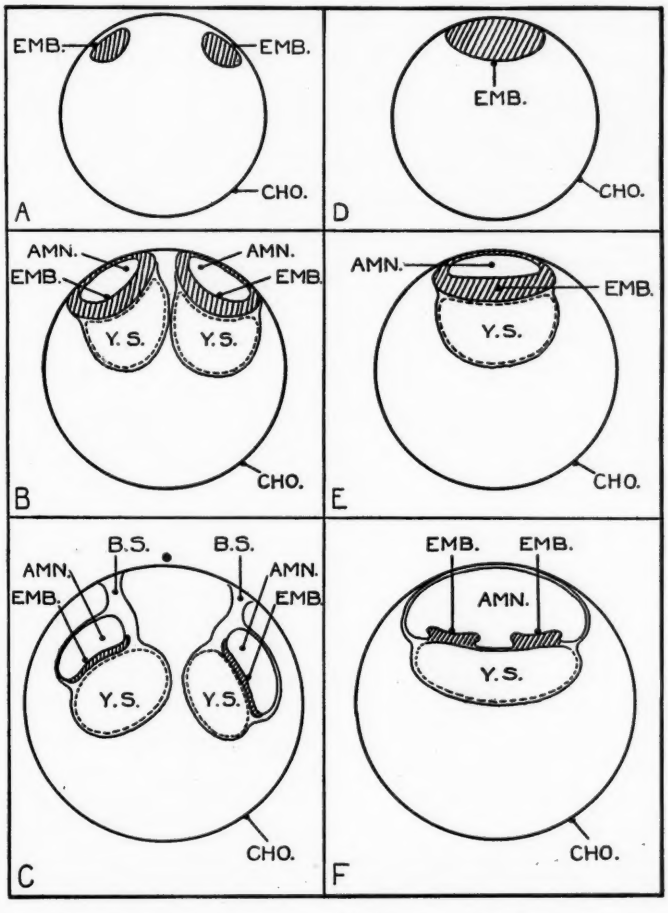


Fig. 7.—Diagrams illustrating two types of single-ovum twinning in man. *A-C*, By formation of two inner cell masses. *D-F*, By formation of two embryos on a single germ disc. (From G. W. Corner, Bull. Johns Hopkins Hosp. 33: 389, 1923.)

(primitive streak stage, Horizon VIII of Streeter's classification). As seen in the opened chorion (Fig. 8, *A* and *B*) one of the embryos looks much smaller than the other; it is in fact somewhat retarded, but the apparent smallness is partly due to folding, and the sections (Fig 8, *D*) show it to be similar in all essentials to its sibling.

*The Mateer ovum (Carnegie No. 1399), which is about the same age as Heuser's specimen, was thought to be a case of twinning by the late G. L. Streeter,[13] who described two little vesicles in the body stalk which he identified as the amnion and yolk sac of a much retarded second embryo. With increasing knowledge of very early human embryos this interpretation has become open to doubt.

This unique specimen is beautifully supplemented by that shown in Fig. 9, which is reproduced by courtesy of Dr. W. R. M. Morton,[15] of Queen's College, Belfast, who has published a brief description of his skillfully prepared specimen. Here again two embryos, about 32 days old, are seen in a single chorion but in separate amnions, each having its own yolk sac. A still

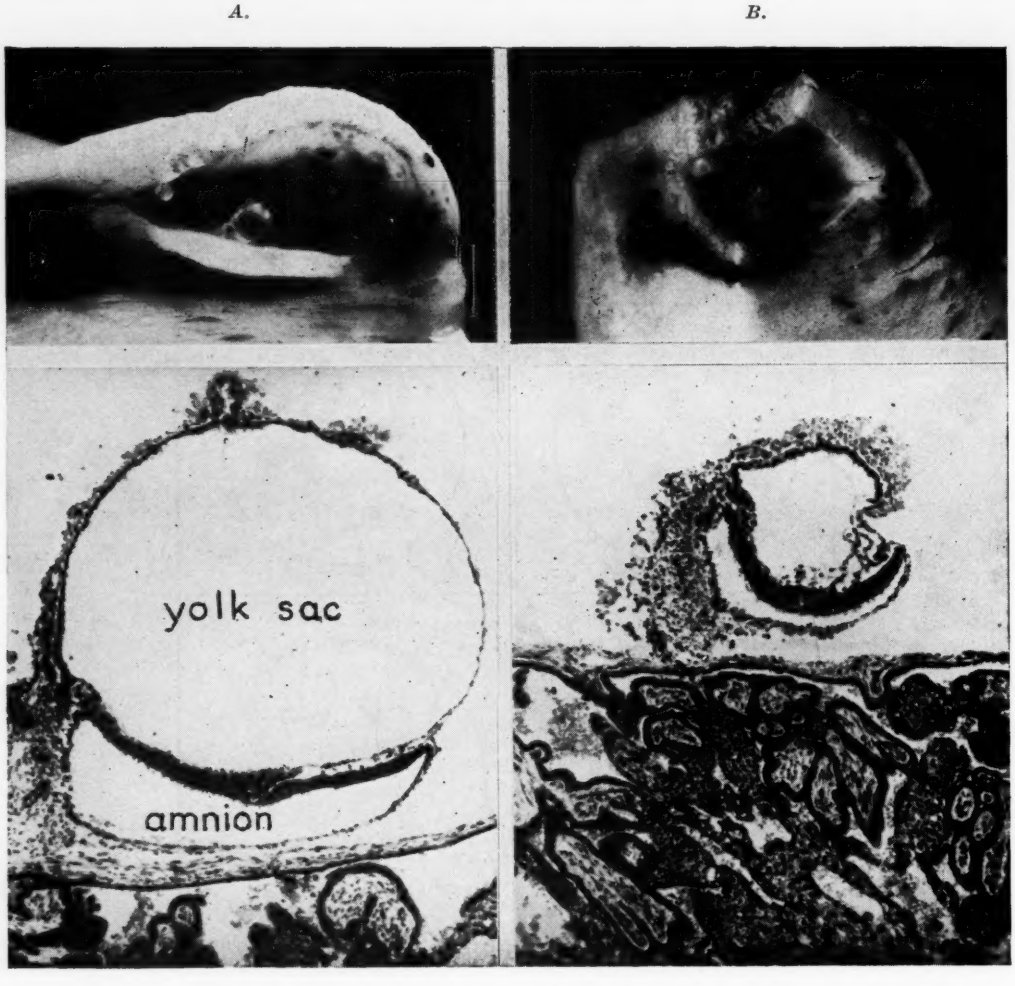


Fig. 8.—Monochorionic twin embryos of about 17 days (Carnegie No. 9009). Above, two views of the opened chorion (×4); below, embryo *A* (left) and embryo *B* (right) (×50).

later stage is shown in Fig. 10, from the case of Dr. Craig Potter[16] sketched under the present writer's supervision at Rochester, N. Y. The Carnegie collection includes a similar but slightly younger specimen (No. 7945) which, however, is not as well adapted to illustration as Potter's. It is easy to visualize the ultimate development of a case of this sort; the two amnions will enlarge until their walls come into apposition, forming a septum which divides the single chorionic cavity into two chambers, each containing a fetus. Obstetricians are familiar with this arrangement as seen at term, when careful

examination of the afterbirth reveals the doubled amnion and permits the retrospective deduction that the two infants must have come from two inner cell masses in one blastocyst.

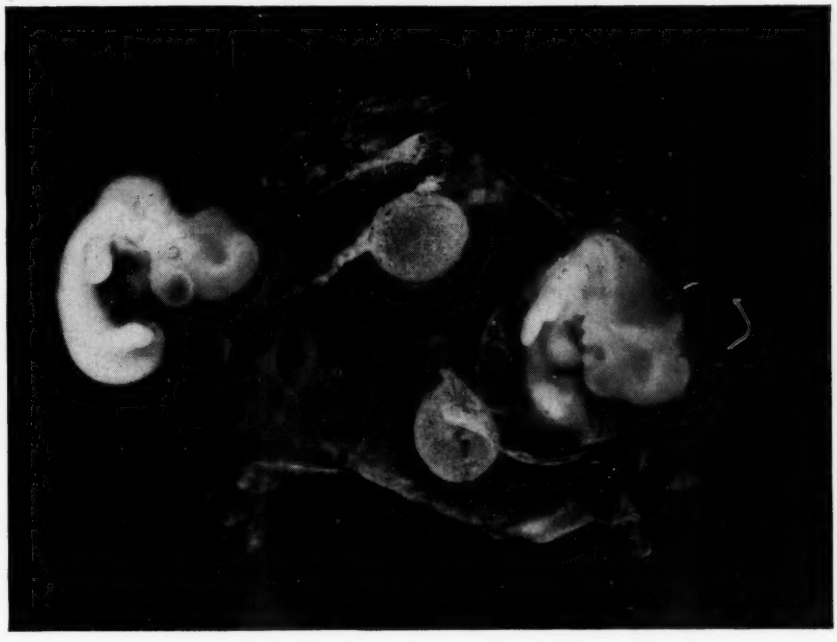


Fig. 9.—Monochorionic twin embryos of about 32 days (11 mm.) (× ca. 2.5.) (By courtesy of Dr. W. R. M. Morton, Queen's University, Belfast.)

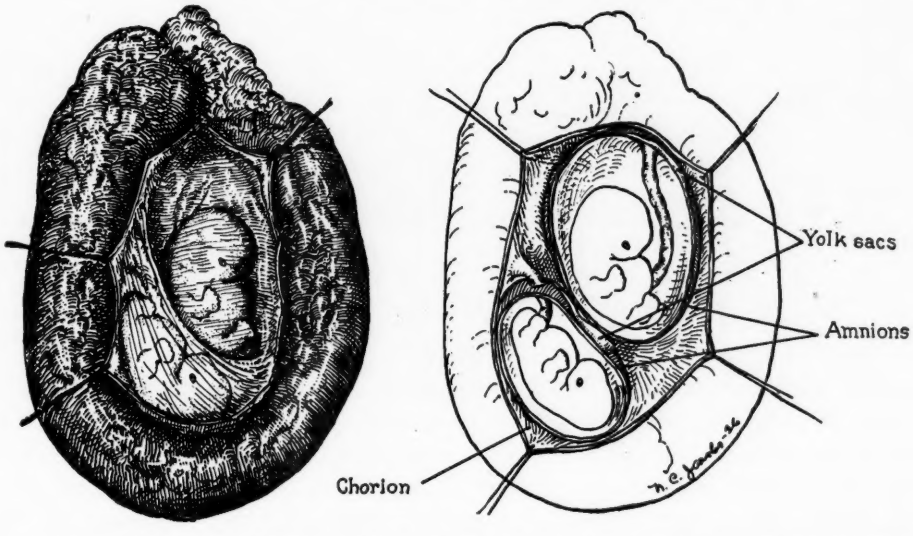


Fig. 10.—Monochorionic twin fetuses of about 5 weeks. (From original of Figs. 1-2, J. Craig Potter, Anat. Rec. 34: 255, 1934.)

A curious variation of this pattern is seen in Fig. 11 (Carnegie collection, No. 6777). In this case a pair of monochorionic embryos is seen, each in its own amnion. There is, however, only one yolk sac. Dr. Heuser, who prepared and recorded the specimen, noted that the yolk sac communicated with

the endodermal cavity of each embryo by the tubular canals which are seen in the photograph. To explain the origin of this arrangement we shall have to resort to conjecture, for there is no earlier specimen of the same kind to help us. At about 11 days after ovulation, i.e., between the stages shown in Figs. 3 and 4, respectively, there is a large "primitive yolk sac" which a few days later contracts to form the small definitive yolk sac. In Fig. 12 a hypothetical case of twinning has been created by putting a second embryo inside the chorion of a single 11-day embryo (Carnegie collection No. 7700). Assuming that the two embryos continue to share the one primitive yolk sac, then the contraction of the latter might easily result in such an arrangement as in Fig. 11. This sort of variation gets the attention of the embryologist rather than of the obstetrician, who would not be likely to discover it at birth, when the yolk sac is inconspicuous or has disappeared.

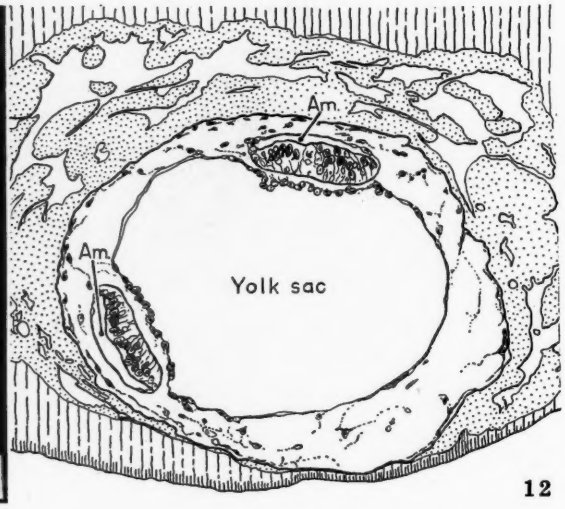


Fig. 11.—Monochorial twin embryos with a common yolk sac, of about 40 days (Carnegie No. 6777). (×1.5.)

Fig. 12.—Diagram showing way in which the twins shown in Fig. 11 probably developed. (A second germ disc and amniotic cavity superimposed upon a section of single embryo of about day 11 (Carnegie No. 7700). (×100.)

III. Duplication of the Embryonic Rudiment of the Germ Disc

The third variety of twinning, latest in time of origin, can best be understood if we return to Fig. 5. At this stage (about 15 days) the body of the embryo is latently present in the germ disc or ectodermal plate, and its location is determined as shown by the rudiments of the embryonic node and primitive streak, which are just appearing. In another day or two the embryo itself will become visible as the neural groove and folds appear. Duplication of the embryonic rudiment may occur at this stage if two embryonic nodes develop instead of one. Speaking in the technical language of general embryology, this is a process of double gastrulation. It is well known in chick embryos at the comparable stage; twin and even triplet embryos on one blastoderm have repeatedly been figured in the literature. When such twin-

ning occurs in man, it will follow the pattern diagrammed in Fig. 7, *D* to *F*. Two embryos will appear on the floor of one amniotic cavity, and will have a common yolk sac. This arrangement will persist until birth, when the obstetrician will find two infants in a single chorioamniotic chamber.

In spite of the recognized occasional occurrence of this arrangement at term, I am unable to present a satisfactory illustration of an early embryonic stage of this kind of twinning, with normal embryos. Dr. C. H. Heuser noticed that in one of the Carnegie presomite embryos (No. 8026, 14 days) there is a little extra tab of ectodermal tissue at one side of the germ disc which may possibly be an imperfectly developed twin embryonic area. Gruenwald[17] reported the youngest sure case known to me; his two embryos were clearly in one amnion, but they were badly damaged and the case is a peculiar one at best. The better preserved sibling had 18 somites and the pair was therefore about 24 days old. The best specimen the Carnegie collection can furnish

Fig. 13.—Double monster in intact amnion with yolk sac. Chorion has been removed (Carnegie No. 8233). (×5.)

(No. 7532) is a tubal pregnancy with a pair of macerated embryos that must have been about 11 mm. long (5 weeks) before their death, which probably occurred several days before the operation. The photograph, which is not suited to reproduction, clearly shows the two embryos within a single amnion. This lack of early normal specimens is partly compensated for by the remarkable double monster shown in Fig. 13 (Carnegie No. 8233). Mr. Reather's photograph was made after Dr. Heuser removed the chorion. It shows the two partially united bodies within a single unopened chorionic cavity, below which is the yolk sac. The age of this specimen, which was presented by Dr. John G. Murray, Jr., of Baltimore, is 28 to 30 days (Horizon XIV). It provides absolute proof that twinning may occur after the amniotic cavity has formed. All that is required to visualize, with its aid, a normal case of such

twinning is to imagine the two embryos as quite separate instead of partially fused. Kirchoff[18] had a slightly older double monster in which the two individuals were less closely united (an 11 mm. thoracopagus).

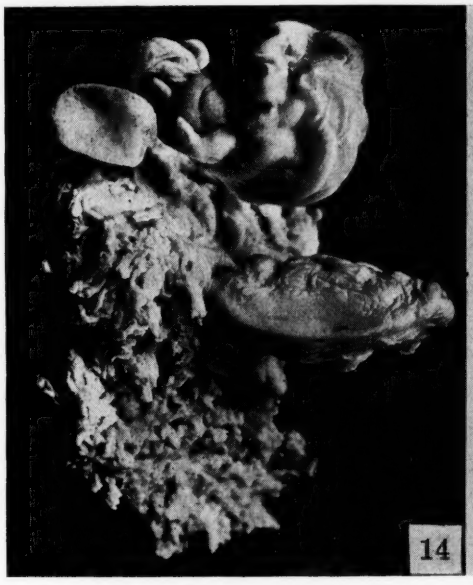
A later case of this sort of twinning is No. 1126 of the Carnegie collection, in which the individuals (12 mm. long; about 6 weeks' gestation age) are quite separate except that they have only a single yolk sac, the yolk stalks branching like a Y (Fig. 14). The information on this specimen is not complete because the amnion had been destroyed by intrauterine maceration or in the process of abortion. Granting that there was only one amnion, the origin of this pair can readily be understood from Fig. 13 by assuming the two embryonic bodies to have developed separately, drawing out the yolk stalk, as they grew, into two channels. The specimen is of historic interest, for Professor L. H. Arey,[19] who studied it while visiting the Carnegie embryological laboratory, reported it in 1922 as the first case which gave proof by direct embryological evidence that human twins may arise from a single ovum. At the time of its discovery the only other illustrative specimens among mammals which Arey was able to cite were Assheton's sheep blastocyst previously mentioned, and the normal developmental stages of the nine-banded armadillo, which will be discussed hereafter.

Fig. 15 shows a later specimen in the Carnegie collection (No. 6290, about 10½ weeks) in which the umbilical cord is single almost to the belly walls of the two infants.

Monoamniotic twinning is considered by obstetricians to be a relatively rare condition. J. K. Quigley,[20] author of a comprehensive review of the subject, found 109 cases in the world literature, to which King, Herring, Witt, and Blood[21] added 5 of their own and 34 from the recent literature, making in all 148 occurrences. The rate of death prenatally or during labor is very high, a majority of the fetal deaths being associated with twisting and entanglement of the umbilical cords. To the embryologist it would appear, from the scanty early material, that the closeness of the two embryos and the consequent difficulty of adjustment of the developing tissues to abnormal configurations of the yolk sac and body stalk must often result in early destruction. This is no doubt fortunate because it reduces the frequency of double or otherwise abnormal individuals and interrupts the development of infants that are doomed to trouble in fetal life or during delivery.

At this point a cautionary statement is in order about the expository plan of the foregoing pages, by which early embryonic development is divided into three stages at which twinning may occur. This is a useful and in the main a factual concept, as the illustrations have shown; but development is of course continuous, and twinning may well begin also in the intermediate phases. Sometime in the segmentation stage, perhaps when the first two blastomeres give rise to four, or at the sixteen- or thirty-two-cell stage, those cells which are to form the inner cell mass are differentiated from the others. Some accident of growth, for example, faulty division of a cell or two at the middle of the little group of embryo-forming cells, might split the tiny germ into two, before it is anatomically distinguishable as an inner cell mass. Thus

two contiguous or only partially separated inner cell masses might arise. Such a condition would be shown diagrammatically in Fig. 7, *A*, if the two inner cell masses were pushed together. It is easy to imagine bizarre consequences, for instance, formation of two amniotic cavities with only one yolk sac. This would give a possible alternative explanation for such a case as that shown in Fig. 14. There might be two yolk sacs with one amnion and one embryo (although no actual occurrence of this kind is known to me). The amniotic and yolk cavities might both be double at first, later becoming fused as the products of the two inner cell masses overcrowded each other. The range of actual possibilities can be determined only as we get more and more complete cases of early twin embryos.



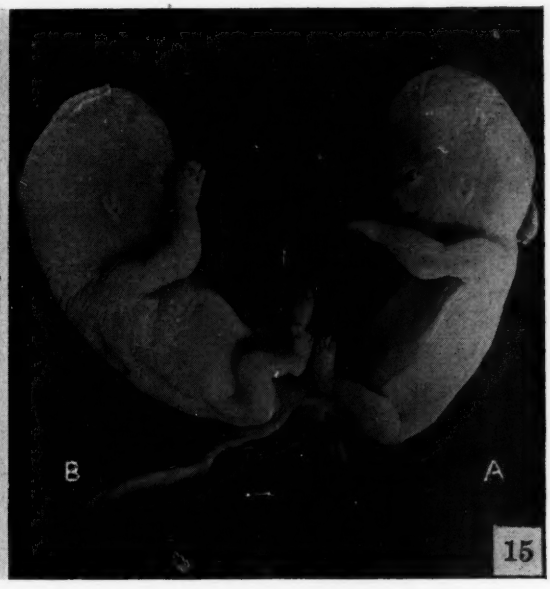


Fig. 14.—Monochorionic and presumably monoamniotic twin fetuses with common yolk sac, of about 6 weeks (Carnegie No. 1126). (× ca. 2.5.) (From original of Fig. 1, L. H. Arey, Anat. Rec. 23: 245, 1922.)

Fig. 15.—Twin fetuses of about 6 weeks with common umbilical cord (Carnegie No. 6290). (×1.1.)

The transition phase between our second and third stages, i.e., during the differentiation of the germ disc from the inner cell mass, also is a possible time for the onset of twinning. The cellular pattern of duplication of the primitive streak might be present early enough, for all we know at present, to cause variation in the subsequent development of the yolk sac and body stalk. We must suppose that the range of duplication of the umbilical cord from a short-limbed Y, as in Fig. 15, to complete duplication of the cord, as in cases shown by King, Herring, Witt, and Blood,[21] results from continuous variation of the time of first duplication of formative cell groups rather than from a discontinuous series of stages such as we found convenient for expository purposes. One can imagine, for example, that exceptionally wide spacing between two incipient primitive streaks, determined early, might cause the

development of two definitive yolk sacs instead of one, so that each infant would have its own yolk sac, just as if each one had arisen from a separate inner cell mass.

Though hypothetical, this is a matter of some importance, because the thought has occurred to more than one student of multiple births that the degree of resemblance between one-egg twins may depend, in part at least, upon the amount of cellular differentiation that has taken place before twinning begins. By the time when the primitive streak forms, the right- and left-sidedness of the germ disc is fixed, and one embryo of a twin pair arising at this stage may get more, the other less of the right-side material. They would then differ in the same way that a portrait of a human face differs if split and recombined into two pictures, one made up of two right sides and the other of two left sides. The fact that Siamese twins are usually slightly different has been hypothetically explained in this way. As already pointed out, Siamese twins are of the late-forming class; separate twins of similar origin might well differ to the same degree. One difficulty, however, in relating the degree of resemblance to the time of onset of twinning lies in the fact previously discussed, that the pattern of the membranes at birth may not be a closely accurate index of the stage at which the differentiation of the two embryos began to diverge.

The question has often been raised, whether the information about the type of twinning, given us by examination of the placenta and membranes, is reliable in view of the possibility of deceptive fusion of the membranes and even of the conversion of two chorionic or amniotic cavities into one by disappearance of the membranous wall between them. Two placentas can certainly form a single mass, and the adjacent chorionic walls of a pair of double-ovum twins may blend into one layer and thin out so much as to give the impression to the unaided eye that only amniotic tissue is present. For this reason microscopic examination of the membranous wall is necessary before the absence of chorionic tissue may safely be accepted. The total disappearance of chorionic tissue, converting dichorionic into pseudo-monochorionic twins, is to say the least uncommon in intrauterine pregnancies. Vermelin and Ribon[9] reported 109 cases of ostensibly monochorionic twins observed at the Maternité of Nancy, in every one of which the two infants were of the same sex. If any significant number of these cases had been originally dichorionic, then some of the twin pairs would have been bisexual. The possible exceptional occurrence of pseudo-monochorionic twins cannot, however, be altogether dismissed. Arey (1922) described cases of tubal pregnancy which he interpreted as demonstrating fusion of the chorions with subsequent disappearance of the wall between the two originally separate cavities. In the marmoset *Oedipomidas geoffroyi,* as Wislocki[22] has shown, two eggs are shed at each ovulation, giving rise to twin embryos, with fusion and ultimate disappearance of the apposed chorionic walls, leaving the two amnions in an apparently single chorion.

Whether or not in human intrauterine multiple pregnancies the amniotic cavities may secondarily unite by disappearance of the apposed parts of the

amniotic walls is again doubtful. If such union does occur its frequency will ultimately be ascertained by thorough study of monoamniotic twinning as more and more specimens become available. If in any large proportion of such cases seen at birth the cords arose at widely distant points in the placenta, or if in any case remains of an amniotic septum were seen, secondary union of the amniotic sacs would be indicated. In the 5 cases seen and carefully reported by King and associates,[21] 2 of which were also examined by the experienced anatomist Cummins, the cords arose very close to each other, and in the 4 of them in which a specific statement was made about the amnion, there was no sign that an amniotic septum had existed earlier in development. It is highly probable that all 5 cases were monochorionic from the start, originating as shown in Fig. 7, *D, E, F.*

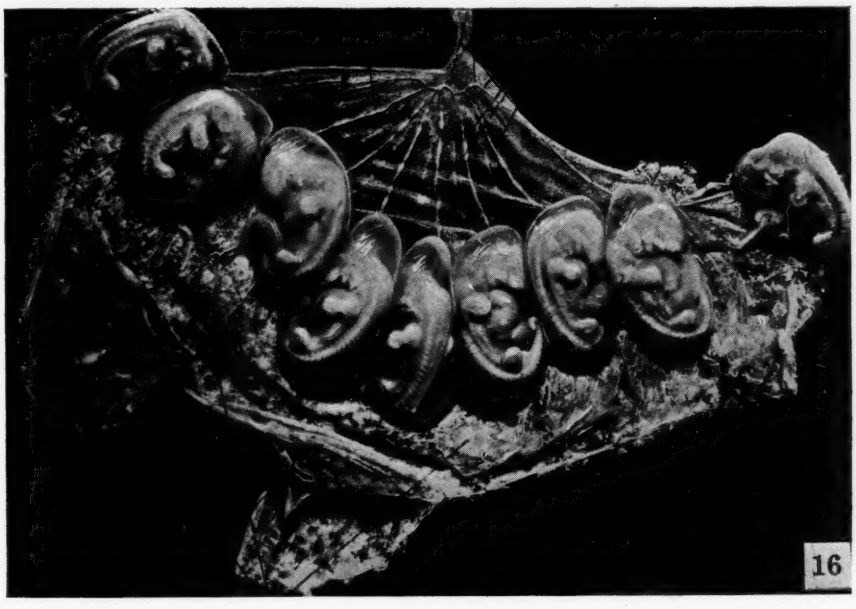


Fig. 16.—Single-ovum nonaplets of *Tatusia hybrida.* Note the individual amniotic chambers communicating by slender ducts with the original site of amnion. (× ca. 2.2.) (After Fernandez, by permission of Museo de La Plata.)

Present evidence indicates that secondary conversion of the chorioamniotic cavities of double-ovum twins, or of two amniotic cavities of a pair of monochorionic twins, into single cavities rarely happens. It follows that the placenta and membranes, if subjected to skilled examination, including microscopic study of the chorioamniotic walls when necessary, will generally yield a correct impression of the type of twinning.

Although, as we have seen, monoamniotic twinning is relatively uncommon in man, there is in the southwestern United States an animal, the nine-banded armadillo, *Tatusia novencinctus,* which regularly gives birth to single-ovum quadruplets in a single amnion. The embryological process can be understood from Fig. 7, *F,* if we visualize four embryos instead of two, i.e., another pair at right angles to the plane of the paper. In the armadillo the

four embryos move farther and farther apart, each drawing out its own part of the amniotic chamber as it moves. The amnion ultimately becomes a branched affair with a central hub at the site of the original amniotic cavity. This has been well described by Newman and Patterson.[23] Another species of armadillo (*Tatusia hybrida,* in Argentina called "mulita") exhibits the most remarkable polyembryony of all, for here the single germ disc gives rise to a variable number of embryos, from six to nine. As these grow apart to find room within the single chorion, each comes to lie in its own portion of the amniotic cavity at the end of a long amniotic duct radiating from the original site of the amnion. Fig. 16, from the monograph of Miguel Fernandez,[24] shows one of these extraordinary gestation sacs, containing in this instance nine embryos, which are single-ovum "nonaplets."

Since twinning of this type, i.e., by duplication of the primitive streak, occasionally occurs in man, we may expect that triplets and still higher multiple births may occur in the same way. There are as yet, however, no embryonic specimens of human single-ovum triplets, quadruplets, or quintuplets early enough to provide direct information as to their exact mode of formation. Triplets arising on one blastoderm have been seen in hen's eggs (Dareste, cited by Newman[25]); and one case of quadruplets in a mammal (opossum) was described by Patterson and Hartman,[26] in which one egg, normally destined to produce a single embryo, actually formed four, obviously by multiplication of the embryo-forming area at the late blastocyst stage. Human uniovular triplets, quadruplets, and quintuplets could arise in this way as well as from multiple inner cell masses; the disposition of the amnion or amnions would, as in the case of twins, reveal the embryological history of the case.

A discourse on the observed embryology of human multiple births should perhaps stop at this point, for the embryologist has no early specimens of polyembryony beyond twins. Something remains however to be said to the obstetricians about the contribution they can make to the subject. In the case of a triplet, quadruplet, or quintuplet birth we do not have, as with twins, a simple question of single-ovum vs. double-ovum origin; within the group of three, four, or five siblings there may be any combination of single-ovum and double-ovum development. Thus, among 4 recently reported cases of quadruplet birth in which the placentas and membranes were carefully studied, in one the infants evidently came from four eggs (Bowyer and Corner[27]); in another there were three eggs, one of which had formed monochorial twins having separate amnions (Ryan and Wislocki[28]); in another there were two eggs as evidenced by the development of three girls in one amnion with a twin brother having a separate placenta and amnion (Ullery[29]); and in a fourth case all four quadruplets came from one egg (Searle and Denny[30]). When Dr. Norma Ford Walker of Toronto[31] was studying multiple births in connection with the Dionne sisters she gathered together all available information on previously reported cases of quintuplet

gestation. Putting together what could be learned from clinical reports on the placentas and membranes, and from anthropological data such as sex, color of skin, eyes, and hair, fingerprints and bodily measurements, she deduced that, out of 46 cases then known, in 3 the five infants came from one egg; 38 represented all combinations possible with 2 to 5 eggs; and 5 were indeterminable. The 2 cases now on record in which all five quintuplets survived differ as to their presumable zygosity. The Dionne sisters showed such a high degree of resemblance that it is impossible to avoid considering them uniovular. The Diligenti quintuplets, born at Buenos Aires July 14, 1943, are three girls and two boys. Although, as in the Dionne case, confusion reigned at the birth, and the placentas and membranes were destroyed without examination, the midwife who presided over the Diligenti births said that there were at least two placentas. Professor Beruti,[32] to whom we owe what little scientific information there is about these children, reported that the two boys have hair of different shades. In an Associated Press photograph published when the children were about 2 years old the boys looked slightly unlike each other, the girls looked much alike. In this case there were presumably at least three eggs, i.e., one for each boy and one or more for the girls.

This question is not merely an embryologist's puzzle. Children of triplet, quadruplet, and quintuplet births as they grow up can become valuable subjects for the study of heredity, provided that reliable information is available as to their zygotic relation. Those infants that came from one egg have identical genic constitutions; those gestated with them but from another egg are related to them only as are brothers and sisters born of separate pregnancies. Such groups of siblings can therefore give us much information about the relative influence of heredity and environment upon the development of mental and physical traits, and about the inheritance of diseases and of susceptibility to disease.

All cases of twin birth are therefore worth careful study of the placenta and membranes. Multiple births of higher order are still more deserving of such study. Every physician who delivers triplets or quadruplets owes it to medical and biological science to do everything he can to preserve the placentas and membranes. In hospital practice this should always be possible. When, as often nowadays, a multiple birth is diagnosed by x-rays or other means, in advance of delivery, the obstetrician can plan for scientific study at the time of birth. A competent person (an embryologist or embryologically oriented physician when available) should be present with the sole duty of taking charge of the afterbirths. He should be provided with numbered tags to be tied to the umbilical cords, matching the identification tags of the infants, so that each afterbirth will be permanently identified with the corresponding infant. The placentas and membranes should be examined while in the fresh condition only as far as possible without disturbing the anatomical relations between adherent placental masses or chorions; then they should be preserved in 10 per cent formol, and placed in large jars so

that they will not become wrinkled. In handling the Bowyer and Corner[27] case we found it useful to stuff the amnions (gently and not tightly) with non-abosrbent cotton wool in order to keep them distended while they were being fixed by the formol solution. Preserved in this way, they were easily studied later and undistorted blocks of tissue could be cut for microscopic study of the membranes and of suspected fusion zones in the placental masses.

When a multiple gestation comes to an untimely end in the embryonic or fetal stage, the products of conception are as important for science as if they had gone on to birth. All such specimens that come into the hands of clinicians and pathologists are valuable for embryological study. Obviously, the rarest and most instructive specimens of uniovular multiple gestation, those of the first few weeks, will not be recognizable as such until the chorion is opened. Since the properly cautious obstetrician and gynecologist leaves this step in the study of an early conceptus to be carried out in the laboratory, discoveries of really early stages, such as that by Dr. C. H. Heuser illustrated in Fig. 8, will occur only as the result of systematic cooperation by surgeons and pathologists in routinely sending material to the embryologist.

Later and less recondite cases which make themselves evident by the abortion of twin embryos or fetuses, or by findings at laparotomy or in the laboratory, are valuable to the embryologist in proportion to their completeness. Even naked fetuses may yield some little information to the trained observer. If the amnions are intact or sufficiently complete to permit tracing their arrangement, the specimen is more informative. A complete multiple implantation in utero is of course invaluable. All specimens which promise to reveal anything about the embryology of multiple births should be placed promptly, and with the least possible disturbance, in 10 per cent formol for subsequent study, preferably by an embryologist. If operation for intercurrent abdominal or pelvic disease allows the ovaries to be examined, the opportunity to count the corpora lutea should not be neglected. Many years ago the geneticist C. B. Davenport asked me to examine the ovaries of a woman who had unfortunately died of pneumonia a week after giving birth to triplets. In the large maternity hospital where the birth occurred, the placentas and membranes had been expertly examined, and two separate gestation sacs were found, one of them containing twins, the other a single infant. When the anatomist, who was by design not told what to expect, reported two retrogressing corpora lutea of pregnancy in the ovaries, the consonance of findings provided striking evidence of the pattern of triplet formation in this case. The story illustrates the value of teamwork in the study of multiple births. Several of the most valuable recent case reports cited in this lecture have resulted from the collaboration of clinicians with the anatomists at their own medical schools or in the same city. All who join in such a study are sure to reap a rich intellectual reward, for in the whole range of human biology there is no subject which so dramatically combines human interest with insight into fundamental scientific problems.

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THE MIDFORCEPS OPERATION

Preliminary Study of 351 Cases

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IN RECENT years considerable controversy has arisen as to whether the midforceps operation should be eliminated from the obstetrical armamentarium. Eastman[1] reported that the incidence of midforceps at The Johns Hopkins Hospital had been reduced from 1:212 deliveries during the period 1936 to 1940 to 1:1,113 deliveries during the ensuing five-year period. He stated that the proper use of pituitary extract in the correction of faulty uterine contractions was the most significant factor responsible for the reduced frequency of this procedure.

Reid[2] evaluated the experience with posterior pituitary extract at the Boston Lying-in Hospital in inertial labor and stated that, as a consequence, the midforceps operation was performed no oftener than once in 200 deliveries.

D'Esopo[3] maintained that the ideal is to eliminate the procedure as much as possible. He predicted that eventually the difficult midforceps operation would be relegated to obsolescence along with craniotomy, high forceps, and hydrostatic bags. An estimated cesarean section rate of 6.0 per cent would be adequate to eliminate the maternal and fetal trauma resulting from difficult vaginal operations. Jones,[4] referring to the experience at the Charlotte Memorial Hospital, Charlotte, North Carolina, concurs in this opinion.

Steer[5] concluded that the midforceps operation should seldom be performed, basing this upon his observations of 227 cases in which there had been considerable maternal and fetal trauma. Seventy per cent of these, however, were cases of disproportion, whereas only 30 per cent were problems of inertia.

Taylor[6] stated that the selective employment of posterior pituitary extract, x-ray studies of the pelvis, antibiotic therapy, and cesarean section have contributed to the virtual elimination of the midforceps operation at the Colorado General Hospital and the Denver General Hospital. The procedure had been performed only 31 times in a series of 10,005 deliveries, an incidence of 1:324. The following were his conclusions: (1) Midforceps operations carry a prohibitive fetal mortality and morbidity. (2) Midforceps procedures produce undesirable damage to the maternal pelvic structures and are associated with secondary hemorrhage and shock in a high percentage of patients. (3) Posterior pituitary extract, if used properly in the correction of pathologic contractions of the first and second stages of labor, will render many midforceps procedures unnecessary. (4) Cesarean section should be used more frequently. (5) Midforceps operations are rarely indicated in modern obstetrical practice.

Jeffcoate,[7] discussing the place of forceps in present-day obstetrics, remarked, "It has gradually but convincingly been demonstrated that many mid-forceps operations, even though technically possible, are prejudical to the health and life of both mother and child. Difficult mid-forceps operations have therefore become fewer and fewer, the safer alternative of cesarean section being preferred. On the other hand, the number of forceps deliveries has become swollen at the expense of what would have been spontaneous deliveries had the second stage been allowed to continue longer." He summarized the situation by saying that in those instances in which babies previously had been stillborn with forceps, they are now being delivered alive by cesarean section, and those which were born dead as a result of spontaneous delivery are now being extracted alive with forceps.

Despite the apparent overwhelming evidence in favor of the elimination of the midforceps operation, large series of cases have been reported in which the operation has had fairly successful results (Weinberg[8] 1,150 cases; Langman and Taylor[10] 701 cases; Decker, Dickson, and Heaton[11] 547 cases).

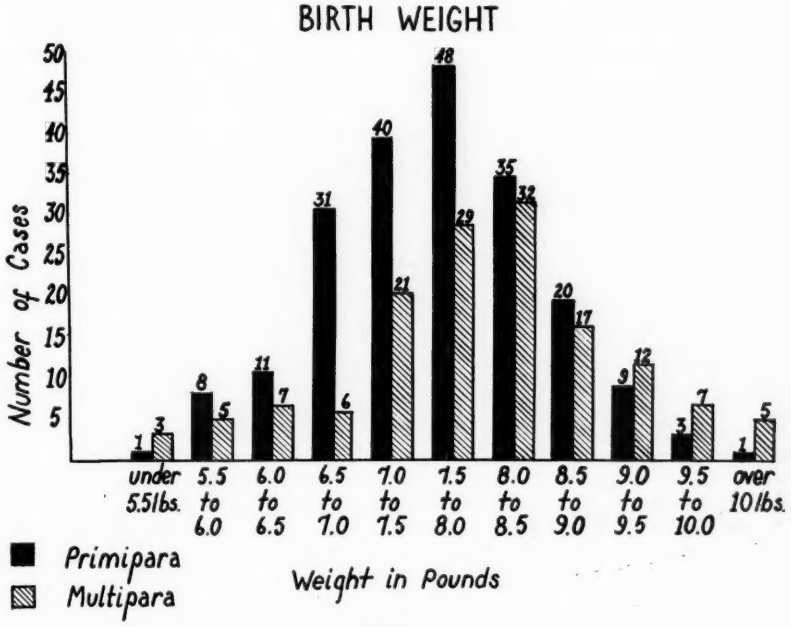

Fig. 1.

Clinical Material at the Hartford Hospital

As a result of the aforementioned conflicting viewpoints, and in an effort to ascertain our position in the controversy, we decided to review the results of the midforceps operations at the Hartford Hospital. Our eventual goal is a survey of ten years' experience. This preliminary report is based upon our observations of 351 cases. Undoubtedly, many cases in which midforceps had been used had been recorded as low forceps and, therefore, are not included. Only those which were recorded on discharge as midforceps are incorporated in this study.

In our cases, there were 207 primiparas and 144 multiparas. The average age of the former group was 25.5 years, the youngest patient aged 16 and the oldest 40. Thirty-six (17.4 per cent) were over 30 years of age. In the multiparous group, the average age was 30.2 years; the youngest patient was aged 18 and the oldest 46. Sixty-eight of these patients were over 30 years of age, 28 over 35, and 11 over 40 years.

The weight of the baby at birth is shown in Fig. 1. The smallest baby in the primiparous group, a second twin, weighed 4 pounds, 8½ ounces. Of the multiparas the lightest baby was 3 pounds, 8½ ounces. The mother was a para i, gravida iii, delivered by the Scanzoni method from an arrested posterior after ten and one-half hours of labor. The heaviest baby in the entire series weighed 11 pounds.

Indications for Midforceps

Table I records the indications for the operation. As noted, 72.6 per cent were performed for arrest in rotation, with prolonged labor accounting for an additional 10.5 per cent. In Weinberg's series of 1,150 cases, arrest was the indication in 92.1 per cent. Rotation had been arrested in 40.8 per cent. Our unclassified group of 7.7 per cent resulted from lack of a specific indication recorded on the charts. This group is analagous to the 5.2 per cent listed by Weinberg as "no indication" in which he incorporated the following: (1) station of vertex misjudged as being lower than it actually was; (2) others delivered because they were prematurely anesthetized to forestall a precipitate delivery; (3) some patients delivered because they were "making such a loud noise or raising such havoc" that, in the absence of contraindications, delivery was expedited.

TABLE I. INDICATIONS

	PRIMIP.	MULTIP.	TOTAL	PER CENT
Arrested posterior	87	77	164	46.7
Arrested transverse	65	26	91	25.9
Prolonged labor	27	10	37	10.5
Fetal distress	13	13	26	7.4
Anterior brow presentation	0	2	2	0.6
Posterior face presentation	0	1	1	0.3
Toxemia	1	0	1	0.3
Prolapsed cord	0	1	1	0.3
Operation for detached retina	0	1	1	0.3
Unclassified	13	14	27	7.7

According to the standard textbooks, a second stage of labor of two or more hours without progress constitutes an indication for operative intervention. In this review, we have deviated from this accepted standard by recording the total duration of labor rather than the length of the second stage. We felt that unless the obstetrician had been in constant attendance on the patient, the approximate time of transition from the first to the second stage of labor could not be recorded with any degree of accuracy. Each of us can recall having been notified by other observers that the cervix had been fully dilated for a considerable time only to find cervix still present upon our own examination.

We admit that in many instances it is also difficult to fix the actual time of the onset of labor. Nevertheless, the establishment of regular uterine contractions affecting the cervix either by effacement or dilatation may be ascertained with a reasonable amount of certainty (Table II).

It is of interest that 57 per cent of the patients had an average labor under eight hours and that 93.7 per cent were delivered after less than twenty-four hours of labor. These figures might lead to speculation as to whether the incidence of operative intervention might have been reduced had labor been allowed to progress spontaneously somewhat longer. Conversely, one might hypothesize that the excellent fetal and neonatal record subsequently referred to in this report might be the direct result of not permitting a fetal head to become wedged tightly in the pelvis for too long a time.

TABLE II. DURATION OF LABOR

	PRIMIP.		MULTIP.		TOTAL CASES		
HOURS	NO.	AV. HOURS	NO.	AV. HOURS	NO.	PER CENT	AV. HOURS
Under 12	83	8.7	117	6.6	200	56.98	7.4
12-16	71	13.8	12	14.0	83	23.64	13.9
16-20	25	18.0	6	18.3	31	8.83	18.0
20-24	15	21.4	4	22.25	19	5.41	21.76
24-28	8	26.5	4	25.25	12	3.42	26.08
28-32	2	28.6	0	--	2	0.57	28.6
32-36	2	32.25	0	--	2	0.57	32.25
Over 36	1	47.0	1	48.25	2	0.57	47.62

Special Procedures and Instruments Used

Table III enumerates the various procedures which had been employed in performing the midforceps operation at this hospital. Conventional types of forceps were utilized in 51 per cent of the cases, the vertex having been manually rotated in 6 per cent prior to the cephalic application of the instrument. The Scanzoni maneuver was utilized approximately three times as often as rotation by Kielland forceps. Barton forceps had been used only twice.

TABLE III. PROCEDURES

	NO.	PER CENT
Cephalic application of conventional forceps	158	45.01
Scanzoni	112	31.9
Kielland rotation	41	11.68
Manual rotation and cephalic application	21	5.98
Wandering blades	14	3.99
Barton forceps	2	0.57
Conversion of brow to anterior face	2	0.57
Rotation of posterior face to anterior	1	0.29

These figures are interesting in the light of numerous reports which recommend the use of a specific type of forceps for each particular indication. Weinberg,[8, 9] Turner,[13] and Mitchell[14] are proponents of this policy. Langman and Taylor summarized the situation by stating that there are two schools of thought regarding the principle to be followed in selecting the appropriate forceps for the management of midpelvic arrest. One group maintains that the operator should be thoroughly familiar with one type of forceps which can be applied in any situation with the vertex presenting. A second school is of the opinion that no forceps is mechanically adaptable to all vertex deliveries. Therefore, special types must be selected for application to particular vertex presentations or to effect delivery through the most favorable diameters of the pelvis. In Langman and Taylor's report of 701 cases, the type of instrument employed was as follows:

Conventional forceps	196
Barton forceps	371
Kielland forceps	134

As a result of their experiences, the following plan was evolved on the Bellevue Service: (1) Conventional-type forceps were used when the head was in the anterior position. (2) With the occiput in the *transverse,* classical forceps were employed if manual rotation to the anterior position could be accomplished easily; otherwise, the Barton blades were utilized to effect descent. (3) The Kielland forceps were the instrument of choice in the *posterior position.*

Ahnquist[15] preferred the Barton forceps for transverse arrest, using them in 43.3 per cent of midpelvic applications. Barton[16] reported his experience with the same forceps in 110 cases. Decker and Heaton[12] analyzed 277 cases in which Barton forceps had been employed. Brougher[17] concluded from his use of the Kielland forceps in 134 of 1,646 deliveries that this instrument did not increase morbidity or infant mortality. Kushner and Wahrsinger[18] reported the use of Kielland forceps in 200 cases with what they considered satisfactory results.

After reviewing our charts, it was evident that each obstetrician had his individual midforceps procedure of choice under the specific circumstances with which he was confronted at the time. The Scanzoni maneuver was utilized frequently for arrested transverse and posterior positions. Apparently the Barton forceps had not attained much popularity with our operators inasmuch as they had been used in only 0.57 per cent of the cases as indicated in Table III.

Maternal Complications

In Table IV, we have classified the maternal complications which resulted from the midforceps operations performed at this hospital. There were 142 complications in 90 (25.6 per cent) of the 351 cases. Analysis of the table reveals the following: 67 complications in 158 cephalic applications of conventional forceps, 42 complications in 112 Scanzoni maneuvers, 26 complications in 41 cases where Kielland forceps were used, and 6 complications in 14 cases where wandering blades were used.

TABLE IV. MATERNAL COMPLICATIONS

COMPLICATION	SCANZONI	KIELLAND ROTATION	CEPHALIC APPLICATION	WANDERING BLADES	BARTON FORCEPS	BROW TO FACE	TOTAL (142)
Sulcus tear	9	10	16	1	-	1	37
Other vaginal lacerations	11	3	22	2	-	-	38
Cervical laceration	5	5	11	1	-	-	22
Dührssen's incisions	-	-	1	-	-	-	1
Bilateral episiotomy	1	-	1	-	-	-	2
Third-degree laceration	-	-	1	-	-	-	1
Hemorrhage	5	1	10	1	-	-	17
Patients transfused	5	1	10	1	-	-	17
Bladder and urethra	2	3	-	-	-	-	5
Phlebitis	-	-	1	-	-	-	1
Urinary retention (over 2 days)	9	4	4	1	-	-	18

There were no maternal deaths in the entire series. An analysis of the complications according to the type of procedure employed discloses that sulcus tears and other vaginal lacerations occurred as follows: with Kielland forceps (31.7 per cent); conventional forceps (24.1 per cent); wandering blades (21.4 per cent); and Scanzoni procedures (17.8 per cent).

Lacerations of the cervix which were sufficiently extensive to require suturing were encountered in 12.2 per cent of the Kielland forceps group, in 7 per cent of the cases when conventional forceps were applied, and in 4.5 per cent when the Scanzoni maneuver was employed.

Inasmuch as the present number of cases in any of the enumerated categories is too small to be of statistical significance, it is our impression that one cannot reach any definite conclusion regarding the relative virtues or disadvantages of any of these procedures. The current figures may reveal a trend perhaps, but only further analysis of a much larger series of cases (as is anticipated) can be of any value.

It is noted with interest that Dührssen's incisions of the cervix had been resorted to but once. There was only one third-degree laceration of the perineum. Bilateral episiotomy had been employed twice. Only eight patients in the series remained in the hospital longer than eight days:

10 days	Urinary retention for 5 days.
11 days	Tear around bladder. Foley catheter for 10 days.
13 days	Sciatic neuritis.
13 days	Urethral laceration. Foley catheter for 11 days.
22 days	Superficial thrombophlebitis.
9 days	Cause not specified (2 cases).
10 days	Cause not specified (1 case).

In order to make a comparison between the incidence of immediate maternal complications in our series and in those of others, a composite of the data contained in eight reports is given in Table V (Ahnquist,[15] Decker and Heaton,[12] Decker, Dickson, and Heaton,[11] Steer,[5] Taylor,[6] Kushner and Wahrsinger,[18] Langman and Taylor,[10] and Weinberg[9]).

TABLE V. TOTAL CASES, 3,198

Maternal mortality	7
Third-degree lacerations	17
Cervical lacerations	150
Dührssen incision	18
Urinary retention	21
Vaginal lacerations	181
Hemorrhage (over 500 c.c.)	184
Vesicovaginal fistula	5
Rectovaginal fistula	1
Thrombophlebitis	1
Fistula in ano	1
Inversion of uterus	1
Laceration of bladder	1
Ruptured uterus	1

The foregoing data make it apparent that even in the most skillful hands the midforceps operation cannot be undertaken without exposing the mother to considerable hazard, especially from cervical and extensive vaginal lacerations with their attendant hemorrhage of such proportions as to necessitate transfusions. While the obstetricians at this hospital have been fortunate thus far in avoiding maternal mortality, the tragic possibility thereof indubitably exists.

Because of the degree of trauma which may be sustained by the maternal soft parts during a midforceps delivery, it is pertinent that an effort be made to ascertain the extent and permanency of the birth-canal injuries. These are represented in Table VI. At this writing, follow-up reports have been obtained of 257 (73.1 per cent) of the cases. Inasmuch as some of the patients had been delivered as recently as six months prior to the initiation of this report, it is conceivable that insufficient time has elapsed for a complete evaluation of the status of the structures of the birth canal. Nevertheless, a general concept can be formulated from the information on hand. From the current figures it is

obvious that the cervix becomes lacerated more frequently than is recognized (24.1 per cent). Furthermore, despite episiotomies, many of which are quite generous, the supports of the pelvic floor appear to be weakened considerably by the procedure. The resultant relatively high proportion of cystocele, rectocele, and prolapse (combined 34.2 per cent) attests thereto.

TABLE VI. MATERNAL FOLLOW-UP

	NO.	PER CENT
Cases reported	257	73.1
Lacerated cervix	62	24.1
Cystocele	40	15.37
Rectocele	37	14.39
Stress incontinence	13	5.06
Prolapse	11	4.26

Strong emphasis has been placed on the role of roentgenographic pelvimetry in either circumventing a traumatic midforceps delivery or facilitating its execution by taking advantage of the most favorable dimensions of the pelvis. It is significant that this valuable adjunct was employed in only 22 (6.3 per cent) of the cases in this series. Perhaps a more extensive utilization of this procedure might have forestalled a certain percentage of the complications which were encountered. On several of the follow-up reports, the comment has been made adjacent to the patient's name, "Should be sectioned next time."

Infant Mortality and Morbidity

One of the principal objections to the midforceps operation is the reputedly high infant morbidity and mortality attending such a procedure. There is a wide range in the reports of stillbirth and neonatal death rates following midforceps operations:

Weinberg[9]	0.8 per cent
Barton[16]	1.8 per cent
Kane and Parker[19]	2.3 per cent
Potter and Adair[20]	5.0 per cent
Acken[21]	5.4 per cent
Erbloh[22]	6.4 per cent
Decker and associates[11]	6.58 per cent corrected to 4.75 per cent
Hoffstrom[23]	6.8 per cent
Kushner and Wahrsinger[18]	7.0 per cent corrected to 4 per cent
Steer[5]	7.0 per cent corrected to 4 per cent
Langman and Taylor[10]	9.4 per cent corrected to 5.2 per cent

Taylor[6] had a most disastrous experience. Eight of his 31 cases (26 per cent) resulted in either a stillborn or an injured infant who succumbed to an injury sustained during birth. An additional 7 infants who were traumatized during birth and survived raised the combined fetal mortality and morbidity to 46 per cent.

Corston[24] reported a stillbirth rate of 8.3 per cent and a neonatal death rate of 5.8 per cent in 323 midforceps deliveries at the Grace Maternity Hospital, Halifax, Nova Scotia. His study further suggested that if a baby survived a midforceps delivery, no physical or mental impairment was to be expected.

At the Hartford Hospital, we have been extremely fortunate in having had only one stillborn in the entire series (0.29 per cent). Actually, the stillbirth rate can be corrected to 0 per cent inasmuch as the fetal heartbeat was not heard when this patient was admitted to the hospital. Therefore, death

could not be attributed to the forceps procedure. Only 2 infants died during the neonatal period. One baby died one and three-quarters hours after delivery from a congenital diaphragmatic hernia and atelectasis. The death of the other was caused by a tentorial tear and subdural hemorrhage which occurred during a difficult midforceps delivery. Therefore, the corrected combined stillbirth and neonatal death rate for this series of cases is the amazingly low figure of 0.29 per cent.

In each of the cases in this report, a questionnaire was forwarded to the responsible pediatrician requesting pertinent information relative to evidences of birth injuries or retarded mental and physical development which could be attributed to the type of delivery. To date, returns have been received on 244 (69.5 per cent). Forty cases are lost to follow-up, not having returned to the original pediatrician. Of the remaining 204 (58.1 per cent) there were only 6 cases in which suspicion could be cast upon the midforceps procedure as a possible etiological factor in any birth injury: (a) One child was slow in physical development. (b) One had Erb's palsy of the left arm from which he recovered completely. (c) One had scissor legs; however, the leg spasm disappeared in one month. (d) One infant had cephalohematomas at birth, but there were no permanent sequelae. (e) One had sustained a laceration of the scalp which was sutured and then healed. (f) One was mentally retarded.

The remaining 198 children were reported as making normal mental and physical progress. Again the question may be raised as to the relatively short period of follow-up (six to eighteen months from delivery). However, if there had been manifestations of permanent brain damage, they could probably have been recognized within this period.

Summary

A preliminary report of the midforceps operations performed at the Hartford Hospital has been presented. The survey has been based upon the experience with 351 cases which occurred in approximately eighteen months; 72.6 per cent of the procedures were for arrest in rotation, and an additional 10.5 per cent for prolonged labor. There was no universal method of delivery. Apparently each obstetrician had his personal preference when confronted with a specific set of circumstances. The Scanzoni procedure was utilized approximately three times as often as the Kielland forceps. Despite the skill of various operators, maternal complications arose in 25.6 per cent of the cases, with sulcus tears, other vaginal lacerations, and lacerations of the cervix predominating.

Follow-up of 73.1 per cent of the cases revealed cervical lacerations in 24.1 per cent and a combined total of 34.2 per cent cystocele, rectocele, and prolapse. Most amazing was a corrected stillbirth rate of zero and a neonatal mortality of only 0.29 per cent.

D'Esopo[3] stated that an estimated cesarean section rate of 6.0 per cent would virtually eliminate all difficult midforceps procedures. At this hospital, however, the cesarean section rate was 8.2 per cent in 1952 and 9.4 per cent in 1953. During eighteen of these twenty-four months, we still delivered 351 babies by midforceps, with a 25.6 per cent incidence of maternal complications. Perhaps the more frequent use of x-ray pelvimetry might have decreased this figure by increasing the number of cesareans.

It is our opinion that the number of cases included in this preliminary report is still too small to be of statistical significance. It is anticipated that the contemplated survey of ten years' experience with the operation will result in the formulation of definite conclusions regarding the procedure.

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RUPTURE OF THE PREGNANT UTERUS

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THE major contributions of antibiotics, blood and fluid replacement, the better understanding of the physiology of labor and pregnancy and improved training have exerted a remarkable influence on all aspects of obstetrics, and sufficient time has elapsed that the effects can be evaluated. The dramatic influence of these advances is clearly illustrated in their role in the acute surgical emergency created by the rupture of the pregnant uterus. At this hospital 8 deaths, 8.5 per cent of the total of 93 maternal deaths from May, 1931, to July, 1953, were due to rupture of the pregnant uterus; all of the deaths occurred prior to July, 1942. Uterine rupture continues to be a serious complication and the occurrence is greater in institutions where mismanaged or neglected cases are accepted.

From May, 1931, to July, 1953 there were 52 ruptures of the pregnant uterus among 71,483 delivered patients, an incidence of 0.07 per cent, which represented one of the higher rates among the reported incidences of other institutions (Table I). Undoubtedly instances of uterine rupture have occurred which were not diagnosed correctly and which were mistakenly considered to be postpartum hemorrhage and shock due to other causes, and in a subsequent pregnancy the uterus may have ruptured again or the laceration may have extended sufficiently to permit detection.

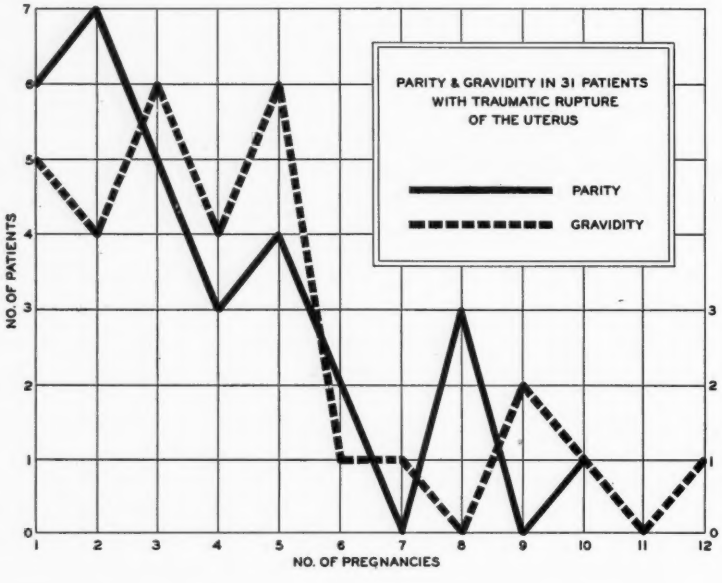
TABLE I. REPORTED INCIDENCE OF RUPTURE OF THE UTERUS IN PREGNANCY

HOSPITAL	YEARS	NO. OF CASES	DELIVERIES	INCIDENCE (%)
University Hospital, Cleveland	1925-1941	23	63,391	0.036
31 Philadelphia County hospitals	1931-1941	105	318,103	0.033
University of Maryland and Baltimore City	1920-1943	45	65,916	0.065
Boston City	1920-1945	44	41,706	0.085
Johns Hopkins	1900-1945	53	53,574	0.099
5 New York hospitals	1932-1946	57	111,753	0.051
Cook County	1920-1948	42	92,226	0.045
New Orleans Charity	1913-1950	96	127,522	0.076
Chicago Lying-in	1931-1953	52	71,483	0.073
Total		517	945,674	
Average Incidence				0.062

The ruptures of the uterus incident to childbirth were customarily classified as noncesarean ruptures and cesarean or postsurgery ruptures, and each group was subdivided into spontaneous, and induced or traumatic ruptures. In this series of 52 cases, 37 ruptures of the uterus were classified as noncesarean ruptures, of which 31 cases were traumatic and 6 cases were spontaneous. Fifteen cases were considered postcesarean ruptures, of which only one instance of traumatic rupture was noted. Such a classification properly emphasized the

unknown integrity of the surgical scar, but it failed, on the other hand, to stress uterine scarring sustained during previous forceps deliveries, intrauterine manipulations, curettages, etc. Another method of classification divided uterine rupture into complete and incomplete ruptures, depending upon whether or not the peritoneum remained intact. The location and extent were of greater importance, however, since rupture and fatal hemorrhage occurred and still remained within the confines of the peritoneum.

TABLE II



There were 6 noncesarean spontaneous uterine ruptures and all 6 of the patients were multiparous and in active labor. The average gravidity was 4.6 and the average parity was 3.1. The past obstetrical histories showed that 2 patients had normal deliveries, but 4 patients gave histories of procedures or conditions, namely, craniotomy, version and extraction, forceps deliveries, and placenta previa with hemorrhage, which could be considered predisposing factors in the ruptures. In 2 patients there was no obstetrical complication at the time of the spontaneous rupture, but in another 2 patients varying degrees of cephalopelvic disproportion were noted. One patient had associated toxemia and uterine prolapse to a degree that during labor the cervix protruded through the introitus, and the other patient had a prolonged labor. Three of the spontaneous ruptures occurred in the lower uterine segment and were incomplete, but 3 spontaneous ruptures involved both upper and lower segments and were complete. There was one maternal death, a mortality rate of 16.6 per cent, which resulted from sepsis with pulmonary and cerebral emboli on the forty-second postpartum day. Four infants were either stillborn or died in the neonatal period, a mortality of 66.6 per cent, and the causative factor was anoxia in all instances.

There were 31 traumatic ruptures of the pregnant uterus. Approximately 65 per cent were in the third and fourth decades of life and the age range was 20 to 45 years. As shown in Table II, 6 patients (19 per cent) were primiparous, which included 5 primigravidas, and 7 patients (22 per cent) were secundiparous. Approximately 81 per cent of the patients had delivered one or more term pregnancies but only 33 per cent of the patients had more than 4 term preg-

nancies. Undoubtedly previous gestations disposed to changes in the myometrium, but antecedent injuries due to instrumentation and manipulation showed a similar correlation of probably greater importance. In Table III, the past obstetrical procedures and complications of labor were compiled for the 31 traumatic uterine ruptures, and in the 26 cases with adequate obstetrical histories 14 patients, 54 per cent, had previous gynecological or obstetrical instrumentation or manipulation which could be considered a predisposing factor in the subsequent rupture.

TABLE III. NONCESAREAN RUPTURE, PAST HISTORY OF PROCEDURES AND COMPLICATIONS

Unknown	6
Spontaneous delivery	79
Forceps delivery	11
Abortion	18
Stillbirth	2
Version and extraction	1
Craniotomy	1
Breech extraction	1
External version	1
Cephalopelvic disproportion	1
Eclampsia	1
Multiple pregnancies, twins	1
Postpartum hemorrhage	2
Placenta previa	1
Prolonged labor	1
Endometritis	1
Uterine suspension	1

TABLE IV. NONCESAREAN RUPTURES, OBSTETRICAL COMPLICATIONS, 1931 TO 1953

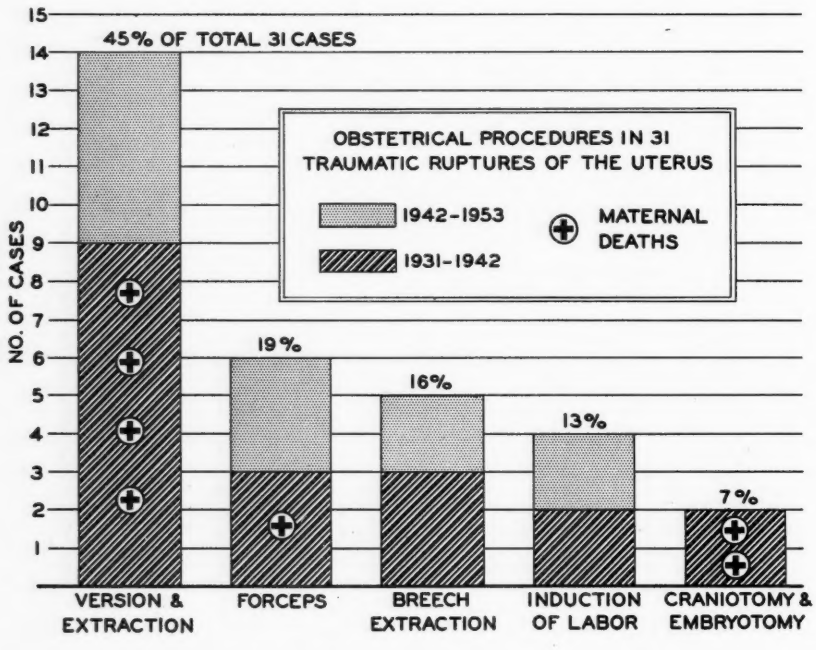
Prolonged labor	1
Prolonged labor with toxemia	1
Prolonged labor with toxemia, breech	1
Prolapse of the cord	1
Prolapse of the cord, polyhydramnios	1
Prolapse of the cord, failure of descent of head	1
Transverse presentation	4
Transverse presentation, prolapse of arm and cord	2
Deflexion attitude	3
Toxemia	2
Placenta previa	2
Abruptio placentae	1
Single footling, breech	2
Breech	2
Persistent occiput posterior	2
Constriction ring dystocia	1
Multiple birth, twins	1
None apparent	3

In Table IV, the present obstetrical complications were enumerated for the traumatic uterine ruptures, and the majority of the conditions required some immediate operative interference by the obstetrician. The most frequent causative procedure in the 31 cases of traumatic rupture was version and extraction, and, as shown in Table V, this procedure was employed in 14 cases (45 per cent) for the following conditions: 4 cases of prolapse of the cord, 2 cases of transverse presentation, 2 cases of placenta previa, one case of prolonged labor, one case of face presentation, one case of brow presentation, and 3 cases of failed forceps delivery. Forceps delivery of any type accounted for 6 uterine ruptures (19 per cent), and of this group 2 cases were considered uneventful low forceps deliveries. Five cases, 16 per cent, resulted from breech extractions and 2 cases, 7 per cent, were attributed to craniotomy or embryotomy.

Oxytocics for induction or stimulation of labor were the causative factor in 4 cases, 13 per cent, and the following case emphasized the limitations and dangers associated with injudicious use of these drugs:

A white woman, aged 40 years, gravida xii, para vii, at term, was admitted because of vaginal bleeding. The past obstetrical history showed 7 normal deliveries and no gynecological surgery. The diagnosis of placenta previa was considered and the membranes were artificially ruptured. Onset of labor failed to occur after 30 hours and the patient was given 2 courses of Pituitrin in 24 hours, consisting of ½ minim for 3 doses at 20 minute intervals. The patient experienced hard pains, chills, fever, nausea, and exhibited hard tetanic contractions during the second course of Pituitrin induction. She delivered spontaneously a stillborn fetus that weighed 3,230 grams one hour and thirty minutes after the initial injection (second induction) of Pituitrin with a blood loss of 275 c.c. A cervical laceration was repaired. Forty-five minutes after delivery the patient went into shock and there was a mass palpable in the left lower quadrant displacing the uterus. Laparotomy showed a complete rupture from a point below the left round ligament to the uterocervical junction. A subtotal hysterectomy was performed and the postoperative course was uneventful.

TABLE V



In Table VI, all traumatic ruptures involved the lower uterine segment and one extended to involve both upper and lower portions. Twenty-two ruptures were incomplete and 9 were complete.

Among the 31 patients with traumatic rupture of the uterus there were 7 maternal deaths, an incidence of 22.5 per cent, and the primary cause of death in 6 cases, 86 per cent, was hemorrhage, as summarized in Table VII. The other maternal death resulted from anuria, due to an incompatible blood transfusion, and terminal bronchopneumonia. Eighteen fetal or neonatal deaths, an incidence of 56 per cent, occurred among the 32 delivered babies, including one set of twins. Of this number 2 infants were previable (below 1,000 grams) and 3 infants had an anomaly which was considered incompatible with life, namely, hydrocephalus, and this group of 5 infants was eliminated for a corrected mortality of 40 per cent. There were 7 intrapartum stillbirths as a result of anoxia and 4 infants died as the result of intracranial hemorrhages which

occurred during delivery by version and extraction in 3 instances and breech extraction in one case. In one instance the cause of death was pneumonitis and in the last case the cause was unknown.

TABLE VI. SITE OF UTERINE RUPTURE

	NONCESAREAN		CESAREAN SECTION	
	SPONTANEOUS	INDUCED	SPONTANEOUS	INDUCED
Cervix and Lower Segment.—				
Incomplete	3	22	4	1
Complete	0	8	1	
Upper Segment.—				
Incomplete	0	0	3	
Complete	0	0	2	
Both.—				
Incomplete	0	0	1	
Complete	3	1	3	
Total	6	31	14	1

Postcesarean uterine rupture occurred in 15 patients, but of this group 6 cases should be considered as separation of the previous cesarean scars, since the ruptures were asymptomatic and recognized only at the time of the repeat cesarean sections. The asymptomatic separations of the previous cesarean scars resulted in no maternal or fetal deaths, and occurred in sites of 3 previous classical sections, 2 laparotrachelotomies, and one hysterotomy. As shown in Table VII, in the group of 9 true uterine ruptures 4 patients had previous classical sections, 3 patients had previous low cervical sections, and in 2 patients the type of section was unknown. The gestation ranged from 32 to 42 weeks, and all of the patients were in active labor for a duration of one to twenty-four hours. Uterine tenderness was the most reliable sign of rupture and some degree of vaginal bleeding was present in 6 cases. In one instance the cause of the rupture was trauma which resulted from a midforceps delivery after a twelve-hour labor. In another instance a patient was given a three-hour test of labor and vaginal examination showed an incomplete laceration at the site of the previous low cervical section. There was no maternal mortality but 6 fetal deaths occurred in the group of 9 true uterine ruptures. One infant died of congenital heart disease but the other 5 deaths, a corrected mortality of 55.5 per cent, were the result of anoxia associated with complete uterine rupture in 3 previous classical scars, one previous section of unknown type, and one previous low cervical section.

Diagnosis and Management

The signs and symptoms of uterine rupture varied according to its type and location. In this series, the classical signs and symptoms of rupture, as abdominal pain and tenderness, cessation of labor, and shock were noted only in the spontaneous uterine ruptures. The majority of patients with traumatic ruptures were anesthetized or given sedation and the classical clinical picture was masked. Immediate postpartum hemorrhage and shock were the characteristic signs in 90 per cent of the patients in the traumatic group. Forty per cent of the patients with postsurgery uterine ruptures gave no evidence of impending or actual rupture of the uterus.

The prime requisite for successful management was early diagnosis and active treatment, consisting of adequate blood and fluid replacement, surgical intervention, and liberal use of antibiotics postoperatively. The procedure of choice was hysterectomy, complete or incomplete, which was performed in 40 cases, 77 per cent (Table IX). The uterus was packed in 5 cases and in an additional 3 cases the uterine packing was augmented by clamping the uterine arteries as a terminal procedure. In 2 instances of separation of a previous cesarean scar successful repair was accomplished.

TABLE VII. MATERNAL MORTALITY DUE TO RUPTURE OF THE UTERUS

AGE	UNIT	YEAR	OBSTETRICAL HISTORY			PRESENT COMPLICATION	OBSTETRICAL PROCEDURE	TREATMENT OF RUPTURE	DURATION OF LIFE	CAUSE OF DEATH
			GRAVIDITY	PARITY	LENGTH OF GESTATION					
39	57813	1932	iv	iii	40 weeks	Brow presentation	Version and extraction, manual removal	Subtotal hysterectomy	6 hours	Hemorrhage
34	68220	1932	iv	i	?term ?48 weeks	Membranes ruptured for 37 hours. Sepsis, transverse presentation	Craniotomy Cleidotomy	Packing	6 hours	Hemorrhage and sepsis
26	76849	1933	ii	i	22 weeks	Abruptio placentae. ?Placenta previa	Version and extraction. Craniotomy	Packing. Subtotal hysterectomy	11 hours	Hemorrhage
25	78137	1933	iii	ii	40 weeks	Toxemia. ?Abruptio placentae. Single convulsion. Dilatation 7-8 cm.	Low forceps rotation, manual removal	Clamping arteries, packing	2 hours	Hemorrhage
22	115548	1934	i	0	44 weeks	Intrapartum stillbirth. Labor of 72 hours. Pituitrin and bag induction	Vaginal hysterotomy, craniotomy and embryotomy	Packing and clamps	5 hours	Hemorrhage
35	206129	1938	iii	iv	40 weeks	Prolonged labor, 30 hours. Rupture of uterus recognized (spontaneous)	Low forceps, manual removal	Packing, total hysterectomy	42 days	Peritonitis, septic, emboli, hemorrhage
24	233147	1940	i	0	37 weeks	Toxemia, Voorhees bag induction, 49 hour labor	Version and extraction	Subtotal hysterectomy	24 hours	Hemorrhage and sepsis
24	284357	1942	v	iv	40 weeks	Transverse presentation. Prolapsed arm	Version and extraction	Subtotal hysterectomy	8th postoperative day	Anuria and terminal bronchopneumonia due to incompatible blood transfusion

TABLE VIII. CESAREAN SECTION OR POSTSURGERY UTERINE RUPTURE

PARITY	GESTATION WEEKS	PREVIOUS INDICATION	TYPE OF SECTION	LENGTH OF PRESENT LABOR	COMPLICATION	RUPTURE	MANAGEMENT	FETAL OUTCOME
i	42	Placenta previa	Low cervical	3 hours test		Incomplete, lower uterine segment	Repeat section	Infant: living
i	36	Dystocia dystrophy syndrome and toxemia	Low cervical	1½ hours	Previous section	Complete lower uterine segment and upper uterine segment	Subtotal hysterectomy	Infant: anoxia
i	38	Toxemia	Unknown	12+ hours	Previous section	Incomplete, lower uterine segment	Midforceps, packing and transfusion	Infant: congenital heart disease
i	33	Toxemia	Classical	3 hours (home)	Previous section	Complete, upper and lower uterine segment	Subtotal hysterectomy	Fetus: anoxia
ii	35	Contracted pelvis. Shoulder presentation	Unknown	24 hours (home)	Ruptured uterus	Complete lower uterine segment	Subtotal hysterectomy	Fetus: anoxia
1942-1953.—								
i	36	Transverse presentation	Classical	3 hours	Previous section	Complete, upper uterine segment	Subtotal hysterectomy	Fetus: anoxia
i	32	Unknown	Classical	3 hours (home)	Previous section	Complete, upper uterine segment	Subtotal hysterectomy	Infant: anoxia
i	36	Bleeding	Classical	2½ hours	Previous section History of fall	Complete, upper and lower uterine segment	Total hysterectomy	Infant: living
i	38	Abruptio placentae	Low cervical	4 hours	Previous section	Incomplete, lower uterine segment	Total hysterectomy	Infant: living

TABLE IX. SURGICAL MANAGEMENT

RUPTURES	NO.	MATERNAL DEATHS	
		NO.	%
Traumatic.—			
Subtotal hysterectomy	19	4	21
Total hysterectomy	3		
Vaginal repair	1		
Uterine packing	5	1	20
Uterine packing with vaginal clamps on the uterine arteries	3	2	66
Spontaneous.—			
Subtotal hysterectomy	5	1	20
Total hysterectomy	1		
Cesarean Scars.—			
Subtotal hysterectomy	9		
Total hysterectomy	3		
Vaginal repair	1		
Repeat cesarean section (repair)	2		

Comment

It is evident that every obstetrical procedure or condition is associated with an irreducible minimal hazard of uterine rupture and it is also evident that most uterine ruptures are produced by failure to heed time-tested indications and conditions required for every obstetrical procedure. Using the strictest criteria in analyzing the 52 cases, one may speculate that the 31 traumatic uterine ruptures (88 per cent) in the noncesarean group would have preventable factors.

Version and extraction is the cause of 45 per cent of the traumatic ruptures, and to attempt it in the presence of an incompletely dilated cervix, prolonged ruptured membranes, protracted labor, or after failed forceps invites disaster (Table V). It is of significance to note that in 85 per cent of the uterine ruptures associated with version and extraction the operative procedures have been performed by the resident staff, who have had little or no previous experience. Dieckmann believes that every resident should be trained in version and extraction by electively performing this procedure in selected cases under the direct supervision of a senior obstetrician. The significant observation in Table X is that from the year 1931 to 1942 there were 19 traumatic uterine ruptures with 7 maternal deaths, or 37 per cent, and a corrected fetal mortality of 57 per cent, but from 1942 to 1953, there were only 12 traumatic uterine ruptures with no maternal mortality and a corrected fetal mortality of 15 per cent. The reduction in fetal mortality may be attributed to the corresponding reduction in home deliveries and better supervised labor in the hospital, since 5 of the 12 fetal deaths occurred during home deliveries. The home deliveries may not be considered a contributing factor in the actual maternal deaths, however.

Many factors contribute to the improved management and one important factor is the reduction of the actual incidence of traumatic rupture from 0.06 per cent to 0.03 per cent. The basic principle of management lies in its prevention, and, whereas the actual number of each type of procedure or complication has remained essentially unaltered, the lowered incidence of traumatic rupture may be attributed to the improved management of labor, experience and judg-

TABLE X. SUMMARY OF DATA ON TRAUMATIC RUPTURE OF THE UTERUS

	1931 to 1942			1942 to 1953			1931 to 1953		
Deliveries	30,227			41,256			71,483		
Number of cases	19			12			31		
Incidence	0.06%			0.037%			0.04%		
Maternal Deaths	7		37%	None			7		22.5%
	Hemorrhage		5						
	Sepsis		1						
	Anuria		1						
Fetal and Neonatal Deaths	12		62%	6		46%	18		56%
	Corrected:		58%	Corrected:		15%	Corrected:		40%
Home deliveries 6,668									
Number of ruptures	6 (5 fetal deaths in group)			None (Discontinued, April, 1943)			6		
OBSTETRICAL PROCEDURES	TOTAL	NO.	INCIDENCE %	TOTAL	NO.	INCIDENCE %	TOTAL	NO.	INCIDENCE %
Version and extraction	275	9	3.3	269	5	1.8	544	14	2.6
Breech extraction	967	3	0.3	1,164	2	0.17	2,131	5	0.23
Induction of labor (any type)	2,425	2	0.08	746	2	0.07	3,171	4	0.075
Forceps (any type)	9,301	3	0.3	25,860	3	0.01	35,161	6	0.02
Craniotomy	2								
Time Interval for Recognition of Rupture.—									
Within 30 minutes	42%	8		67%	8		52%	16	
30 to 60 minutes	10%	2		16%	2		13%	4	
60 to 120 minutes	10%	2		8%	1	(2 hours, 23 minutes)	9%	3	
120 and over	38%	7		8%	1	(1 hour, 6 minutes)	26%	8	

ment of the operator, and changing indications for cesarean section due to lowered risk which at this institution has an associated maternal mortality of less than 0.1 per cent and stillbirth and neonatal (uncorrected) mortality of approximately 4.1 per cent. Another factor is the more rapid diagnosis and institution of treatment in which the time interval between occurrence and recognition is within sixty minutes in 83 per cent of the cases in the years 1942 to 1953, and in only 52 per cent of the cases in the years 1931 to 1942 (Table X). One of the standard routines of the delivery room has been the continued observation on the labor room floor of all patients with pulse rates in excess of 100, altered blood pressures, or with a difficult operative delivery or postpartum bleeding. Furthermore, the innocuous manual exploration of the uterine cavity is an essential part of the examination and inspection of the genital tract following a traumatic or normal delivery. Studies in our hospital demonstrate no increased morbidity from manual exploration of the uterus, and the performance of routine manual exploration on the postpartum uterus after uneventful delivery is a vital part of the teaching program of the resident staff.

From 1931 to 1942, the blood replacement averaged approximately 1,270 c.c., and from 1942 to 1953 the average amount was approximately 1,800 c.c., which represents a considerable increase, and a vital step in the management or prevention of shock. In all cases from 1942 to 1953, chemotherapy or antibiotics have been employed prophylactically, but in therapeutic amounts. Once the diagnosis has been established and blood replacement has been instituted, the treatment of choice is immediate operative intervention and in most instances a

subtotal hysterectomy is the procedure of choice since rapid control of hemorrhage with minimal trauma is of extreme importance. All of the cases of spontaneous noncesarean rupture occurred before July, 1942. The same factors as in the traumatic ruptures have played a role in the prevention of the occurrence of spontaneous rupture, but the residency system and the adequate hospital supervision of labor undoubtedly exert the major influence.

TABLE XI. MATERNAL AND FETAL MORTALITY IN RUPTURE OF CESAREAN SECTION SCAR

	1931-1942	1942-1953	1931-1953
Number of cesarean sections	1,592	2,057	3,649
Number of ruptures of the uterus	6 (1 induced)	9	15
Incidence	0.38%	0.43%	0.41%
Approximate number of repeat sections	470	771	1,211
Incidence	1.3%	1.1%	1.2%
Maternal mortality	None	None	None
Fetal mortality*	4 67% (3 anoxia) (1 congenital heart disease)	2 20% (2 anoxia)	6 37%
Corrected:	50%	Same	31%

*All fetal deaths associated with complete uterine ruptures.

TABLE XII. MATERNAL AND FETAL (UNCORRECTED) MORTALITY

	NONCESAREAN (37)		CESAREAN (15)	
1931 to 1942	*Spontaneous (6)*	*Induced (19)*	*Spontaneous (5)*	*Induced (1)*
Maternal	1 17%	7 37%	0 00.0%	0 00.0%
Fetal	4 67%	12 62%	3 60%	1 100%
1942 to 1953	*Spontaneous (0)*	*Induced (12)*	*Spontaneous (9)*	*Induced (0)*
Maternal	0 00.0%	0 00.0%	0 00.0%	0 00.0%
Fetal	0 00.0%	6 50.0%	2 22%	0 00.0%
1931 to 1953				
Maternal	1 17%	7 23%	0 00.0%	0 00.0%
Fetal	4 67%	18 58%	5 36%	1 100%

The indication for cesarean section at the present time in approximately 40 per cent of the cases is that of a previous section, and the old adage of "once a section always a section" is strictly adhered to except for the occasional patient who enters the hospital well advanced in labor. There is no question but that a surgical scar alters the integrity of the uterus, and, regardless of the method employed in closure, the scar is united by connective tissue and there is no adequate means of evaluating the adequacy of the scar. The fact that 28 per cent of the uterine ruptures occurred in the postsurgery scar is convincing evidence of the correctness of this policy. The 6 instances of separation of the previous cesarean scar in which there has been no sign or symptom of rupture and recognition has occurred only at the time of the repeat section clearly illustrate the impossibility of predicting the quality of the scar and the successful outcome in these cases can be attributed to adherence to this policy. The corrected 55.5 per cent fetal mortality associated with the 9 cases of true cesarean rupture is in sharp contrast with the perinatal mortality of 4.3 per cent in cesarean section. The fact that no maternal deaths have occurred in these 15 cases is no justification for subjecting a woman to the hazards of

possible rupture and the sequelae of severe hemorrhage, especially when there is only a 0.1 to 0.2 per cent mortality associated with cesarean section. There is no evidence to indicate that modern methods of treatment have reduced the frequency of uterine rupture in the cases of previous section, since, as shown in Table XI, the incidence of postcesarean uterine rupture, 1.3 per cent for the years 1931 to 1942, has remained essentially unaltered when it is compared to the incidence of 1.1 per cent for the years 1942 to 1953. It is important to keep in mind that every patient who has had a cesarean section is a potential candidate for uterine rupture at almost any time in the third trimester, since in this series 50 per cent of the uterine ruptures have occurred between the thirtieth and thirty-sixth weeks of gestation.

Summary and Conclusions

From 1931 to 1953 there were 52 cases (0.07 per cent) of rupture of the pregnant uterus among 71,483 delivered patients. The associated maternal mortality was 15 per cent and the uncorrected fetal mortality was 50 per cent.

Uterine rupture remains a serious surgical emergency but there were no maternal deaths in the 21 ruptures which occurred from 1942 to 1953. The contributing factors in the reduction were the following: better understanding of the physiology of labor, hospital delivery, earlier diagnosis, more adequate blood and fluid replacement, immediate surgical intervention, and employment of antibiotics.

Forty-five per cent of the traumatic uterine ruptures resulted from version and extraction. Stricter adherence to the indications and conditions required for the obstetrical procedure and the more liberal use of cesarean section were the most important factors in prevention of rupture.

Fifteen cases of uterine rupture have occurred in patients with previous sections, this being 1.0 per cent of the patients with a previous section who came to term. The policy of once a section always a section is strongly advised.

Prevention by the properly selected obstetrical operation is better than treatment. When a rupture of the uterus is suspected, the management of choice is early diagnosis by manual exploration of the uterine cavity and visual inspection of the vagina, cervix, and lower uterine segment, judicious blood and fluid replacement, and surgical treatment. In most instances a subtotal hysterectomy offers the most rapid control of hemorrhage with minimal trauma.

We wish to express our appreciation to Dr. William J. Dieckmann for his interest and suggestions in the preparation of this paper.

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ELECTIVE INDUCTION OF LABOR USING PITUITRIN

An Evaluation of Routine Elective Induction on a Private Obstetrical Service

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WHILE some excellent recent studies have been reported on the use of Pituitrin in the induction of labor[3, 4, 6-10] I feel it is in order to evaluate further the procedure as it is actually practiced in increasingly large numbers of private cases, subject to a number of varying factors and to the attitudes and abilities of many individual physicians. The hospital from which this study arises has for the past ten years and more done a relatively large number of elective inductions with Pituitrin as a scheduled and routine procedure (Fig. 1), and has kept accurate clinical records documenting this experience. Moreover, it is felt that while recent articles on the subject present cases that have been meticulously handled and studied, they do not include the number of cases necessary for meaningful statistics on certain major complications, for these cases are happily infrequent; nor do they report induced and spontaneous labors side by side so that a comparison can be made.

The present study attempts to describe the results of, and to evaluate the complications arising in, 5,052 inductions in which Pituitrin was used, generally with the adjunct of early amniotomy, over the past ten years, and to compare them with the complications arising in 18,039 spontaneous labors over the same period of time.

As has been outlined by Stone,[1] opinion on the use of Pituitrin has evolved from wholehearted condemnation in the 1920's following a siege of enthusiastic and indiscriminate use with a consequent series of accidents, to present-day opinion ranging from cautious approval in reserved cases to routine elective induction of labor. McCormick[2] describes "Pituitrin—a powerful oxytocic and a very dangerous drug. Must be used with extreme caution if at all! In the hands of a fool it may be most fiendish." Dieckmann[3] states, "It is inevitably followed by increased maternal and fetal mortality and morbidity, regardless of how carefully the cases are selected." Contrarywise, Stone and Tanz,[4] in a carefully studied series of 576 cases in which Pituitrin was used to stimulate or induce labor, recommend the procedure, particularly in patients with breech presentations or eclampsia, and state that the only absolute contraindications are frank cephalopelvic disproportion and grand multiparity. Lubin and associates,[5] who used intravenous Pituitrin in 1,000 cases, state that there have been no reports of uterine rupture attributable to Pituitrin intravenously.

Whether or not labor should be electively induced, irrespective of the method, is the bone of further contention. Erving and Kenwick,[6] reporting 600 elective inductions by amniotomy, state that the procedure is safe and justified in the multigravida but is not advised in the primigravida as a routine procedure. Scott and Harrison[7] reporting on 193 private cases concluded that there is no increased maternal morbidity apparent in induction by amniotomy. Hanley[8] performed amniotomy on 653 private patients including 90 primigravidas with a corrected infant mortality of 0.5 per cent and no cases of cord prolapse. Many current authors take the position of Willson,[9] who states, "Rather than approve the routine induction of labor in normal women because it does not add substantially to the risk for mother or child, we should consider the practice in the light of whether or not it is necessary."

Daichman and Pomerance,[10] in a comprehensive study of 657 private cases, state, "The elective induction of labor has a useful place in present-day obstetrics with advantages to both patient and doctor. If the procedure is applied to the proper patient at the proper time, no serious complications should result." These authors studied the effects of both amniotomy and of Pituitrin.

Technique of Induction

Since the safety and success of any procedure are predicated on the ability and experience of the personnel concerned, it should be stated that the nursing staff of this obstetrical service is well oriented toward elective induction, in regard to close individual observation of the quality of labor and constant alertness for signs of difficulty. Patients are individually assigned to members of the nursing staff, who see that the proper dose of Pituitrin is administered at the proper intervals depending upon the character of labor, and who are responsible for up-to-the-minute written data. Special forms summarizing all pertinent data are completed on each case. Furthermore, most inductions are performed by the physicians who have had considerable experience with the procedure and who use it routinely. It is my observation that this group experiences very few of the failures.

Patients scheduled for induction are admitted the previous evening, are prepared, and given a hypnotic to provide a good night's sleep. The following morning, about 5:30, they are given an enema, and receive the first intramuscular doses of Pituitrin at about 6:30. Breakfast is withheld. During the next hour, they usually receive a dose of barbiturates either orally or intravenously, and the membranes are ruptured by the physician, provided the cervix is favorable. Also, at this time, an evaluation can be made of the effect of Pituitrin in producing contractions—some physicians favoring progressive cervical changes before performing amniotomy, and some having more faith in the ability of the cervix to dilate and foregoing this requisite. In either case, almost all inductions currently combine the use of Pituitrin and amniotomy.

Pituitrin, or less frequently Pitocin, is given in doses beginning at ½ minim, progressing to 2 or 3 minims, given at thirty-minute intervals until labor is well established and then only in doses necessary to maintain labor, always at intervals of thirty minutes or more. Often no more than 2 or 3 doses are required, but 12 or 15 are commonly given. Pitocin is preferred in cases of toxemia or hypertension because of its smaller pressor effect.

Patients who receive Pituitrin or Pitocin intravenously are handled similarly, but always with the constant attendance of a physician. Usually a dilute solution of 0.5 c.c. of the oxytocic agent in 500 c.c. of glucose in water is used, with a small needle in the vein so that a flow accidentally greater than 60 drops per minute will not occur. Labor is followed by rectal examinations repeated as often as necessary and by frequent timing and appraising of contractions. The type and amount of analgesia vary with the physician, as do the anesthetic and the delivery itself; but none of these are altered because of induction of labor per se.

Material and Methods of Study

Clinical records of all obstetrical patients admitted to Providence Hospital over the past eleven years, representing 23,091 deliveries, were made available by the Records Department, whose personnel in addition provided invaluable assistance.

Two separate methods were utilized. The first consisted of reviewing all charts, over a period varying from five to eleven years depending on the complication, in which any of a number of complications were recorded—prolapsed cord, ruptured or inverted uterus, lacerated cervix, premature separation, or postpartum hemorrhage. Each chart was checked for factors other than labor as the possible primary cause. For example, in prolapsed cord, cases of less than 36 weeks' gestation or a fetal weight of less than 5½ pounds were discarded, as it was felt that extreme prematurity or intrauterine death might be more related to the prolapse than would the mode of onset of labor. Likewise the prolapse had to have occurred after labor had been in progress.

After the cases were selected, they were classified first into three groups: induced labor, stimulated labor, and spontaneous labor; each group was then further divided into primigravidas and multigravidas and the numbers in these various categories compared. The relative incidences could be readily calculated on the basis of induced vs. noninduced labors, since the total number of deliveries by these two modes of onset of labor was obtainable from yearly statistics. Because it was desirable to investigate a third large group—those labors stimulated with Pituitrin following a spontaneous onset, for which no monthly or yearly statistics were available—the second method was undertaken. This consisted of a careful personal review of 528 consecutive deliveries during the last few months, and a comparison between the three modes of labor as regards the effects of Pituitrin on the duration of labor, fetal weights, percentage of undelivered patients, persistent malposition, neonatal and maternal complications. An attempt was made to compare only items felt to be reliable, none being made to compare the duration of the third stage, the maternal blood loss, and other such items.

Results

Fig. 1 shows the yearly total of deliveries and the number of inductions in which Pituitrin or Pitocin was used, either with or without the adjunct of early amniotomy. A marked rise in Pituitrin inductions occurred in 1949 and 1950, continuing until the present. This does not reflect a change in availability of the procedure, since elective inductions were routinely scheduled before 1944, but represents, rather, an increase in its popularity. There were a total of 23,091 deliveries during this study period, in 5,052 of which, or 21.9 per cent, labor was induced with Pituitrin or Pitocin, and in 5,833, or 25.2 per cent, of which early amniotomy was performed, the two procedures

overlapping in most of the Pituitrin inductions. Fig. 2 portrays, year by year, the percentages of cases in which labor was induced with Pituitrin (with or without amniotomy) and the percentages in which amniotomy was utilized (with or without Pituitrin). In all cases recorded as inductions, labor was actually induced, not stimulated after it had begun spontaneously.

A separate survey of 528 consecutive deliveries in 1954 showed that labor was entirely spontaneous in 51.3 per cent, induced in 32.2 per cent, and stimulated in 16.5 per cent (Fig. 3). A subdivision of these groups into primigravidas and multigravidas discloses a tendency to induce labor relatively less often in the former. Whereas 26.6 per cent of all these patients are primigravidas, only 17.3 per cent of the inductions are in primigravidas.

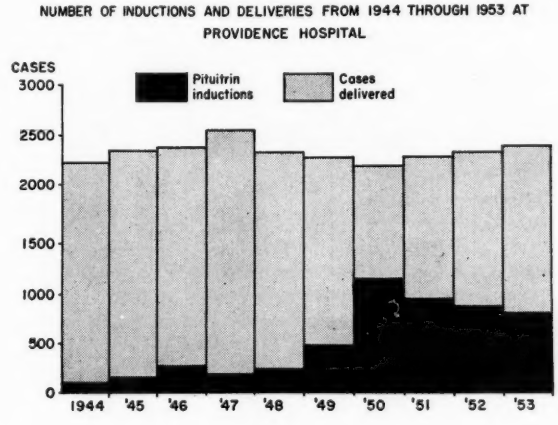

Fig. 1.

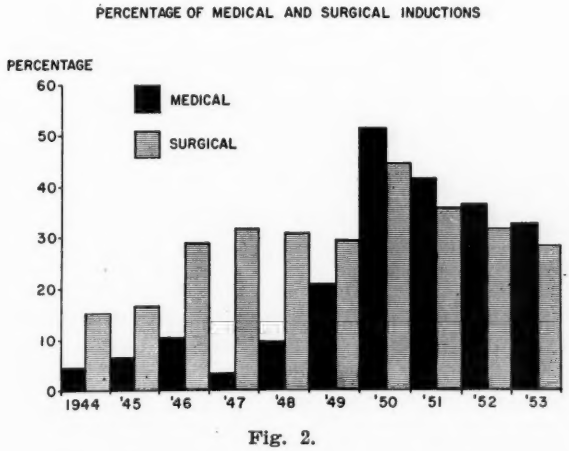

Fig. 2.

The duration of the first stage of labor appears to be shortened by the use of Pituitrin or Pitocin, particularly where labor is induced (Fig. 3, *B*). At least there is a proportionately greater incidence of labors of less than 2 hours' duration. The only primigravidas who had first stages of less than 2 hours were in the group with spontaneous labors. In labors with a first stage longer than 12 hours, the situation is reversed (Fig. 3, *C*). Only primigravidas fall into this category, except in induced labor where there are a few multiparas. The greatest percentage of prolonged first stage falls in the

group with stimulated labor (ineffectual labor being the reason for stimulation), the next in induced labors, and the lowest in spontaneous labor. There appears to be less chance of prolonged labor in cases selected for induction, than in those in which Pituitrin is used to stimulate a labor which is not progressing well.

The duration of the second stage (Table I) parallels that of the first stage closely, though the differences are less marked. The greatest number of cases with a short duration (30 minutes or less) are in the multigravidas and induced labors. Those of long duration (60 minutes or more) are in the primigravidas and in the stimulated labors. Again, Pituitrin appears to shorten the duration of labor.

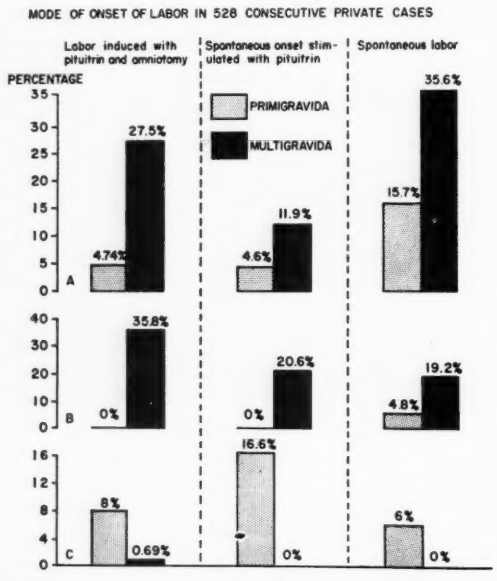

Fig. 3.—*A, Mode of Onset.* The vertical column represents the percentage of cases in which each of three types of labor occurred—induced labor, stimulated labor, and spontaneous labor. These are further divided into primigravidas and multigravidas.

B, Labors of Short Duration. The vertical column represents the percentage of cases in which the first stage was less than two hours in duration. Induced labors result in the highest percentage of short labors.

C, Labors of Prolonged Duration. The vertical columns represent the percentage of labors in which the first stage of labor lasted longer than twelve hours. The highest percentage is in stimulated labors and all but one were primigravidas.

Cases that were not delivered (Table II) for the most part represent false labor in the spontaneous group and failure of induction in the induction group. Cesarean sections are not included in this study. Labor, apparently, fails to ensue more frequently in spontaneous contractions than in induced ones. Although the spontaneous group includes a few cases which were admitted for symptoms other than labor pains, they are probably equaled in the induction group by the small number of cases where attempts at induction were insufficient. Admissions for reasons other than delivery (toxemia, etc.) were not included. Primigravidas predominated in failed inductions, whereas multigravidas predominated in false labors—particularly those where stimulation with Pituitrin was attempted. Induction was successful in 97.2 per cent of multigravidas and in 96 per cent of primigravidas.

Persistent posterior, and transverse positions appear to have had a high incidence in primigravidas where stimulation was used (Table II).

TABLE I. DURATION OF SECOND STAGE OF LABOR IN 528 CONSECUTIVE CASES

DURATION	LABOR INDUCED		LABOR STIMULATED		LABOR SPONTANEOUS	
	PRIMIGRAVIDAS %	MULTIGRAVIDAS %	PRIMIGRAVIDAS %	MULTIGRAVIDAS %	PRIMIGRAVIDAS %	MULTIGRAVIDAS %
60 minutes or more	32	2.8	45.8	4.8	48.3	2.6
30 to 60 minutes	48	18.6	45.8	14.3	25.3	20.7
30 minutes or less	12	77	8.3	73	21.7	67

The percentages represent, for each mode of labor, those falling into the three time categories. The sum in each column is 100 per cent minus the sections and undelivered labors. The use of Pituitrin to induce or stimulate labor has some tendency to shorten the second stage.

TABLE II. PERCENTAGE OF CASES DISCHARGED UNDELIVERED IN 528 CONSECUTIVE CASES ADMITTED

	LABOR INDUCED		LABOR STIMULATED		LABOR SPONTANEOUS	
	PRIMIGRAVIDAS %	MULTIGRAVIDAS %	PRIMIGRAVIDAS %	MULTIGRAVIDAS %	PRIMIGRAVIDAS %	MULTIGRAVIDAS %
Patients discharged undelivered	4.0	3.5	0	7.9	4.8	8.5
Persistent posterior and transverse positions	4.0	3.4	16.7	3.2	3.6	4.8

Failure to complete labor and delivery occurs less often in induced than in stimulated or spontaneous labors. In the primigravida, there is a high incidence of malposition in stimulated labors.

TABLE III. BIRTH WEIGHTS OF INFANTS IN 528 CONSECUTIVE PRIVATE CASES

WEIGHT	INDUCED				STIMULATED				SPONTANEOUS LABOR			
	PRIMIGRAVIDA		MULTIGRAVIDA		PRIMIGRAVIDA		MULTIGRAVIDA		PRIMIGRAVIDA		MULTIGRAVIDA	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Less than 5½ pounds	1	4	2	1.4	0	0	6	9.5	4	4.8	22	11.7
5½ to 6½ pounds	2	8	22	15.2	5	20.8	7	11.1	14	16.8	29	15.4
6½ to 8½ pounds	20	80	98	67.6	18	75	37	58.8	55	66.4	106	56.4
8½ pounds or more	1	4	18	12.4	1	4.2	8	12.7	6	7.2	15	8
Undelivered	1	4	5	3.5	0	0	5	7.9	4	4.8	16	8.5
Total	25	100	145	100	24	100	63	100	83	100	188	100

The birth weights of infants in this series are shown for each of the three types of labor in Table III. The incidence of premature infants (less than 5½ pounds), as shown in Table IV, is less when Pituitrin is used than when not used. These differences are also borne out in the case of "underweight" infants (5½ to 6½ pounds), though to a smaller degree, as shown in Table V.

TABLE IV. PERCENTAGE OF INFANTS WEIGHING LESS THAN 5½ POUNDS IN 528 CONSECUTIVE PRIVATE CASES

Induced labor	1.77%
Spontaneous or stimulated labor	8.94%
Pituitrin used to induce or stimulate	3.5%
Pituitrin not used	9.6%

Prolapsed cord was recorded in 54 cases out of 20,890 deliveries over a nine-year period—an incidence of 0.258 per cent (Table VI). The incidence in induced labors is 0.465 per cent as compared with 0.195 per cent in spontaneous labors.

TABLE V. PERCENTAGE OF INFANTS WEIGHING BETWEEN 5½ AND 6½ POUNDS IN 528 CONSECUTIVE PRIVATE CASES

Induced labor	14.1%
Spontaneous or stimulated labor	15.4%
Pituitrin used	14.0%
Pituitrin not used	15.9%

TABLE VI. CASES OF PROLAPSED CORD IN 20,890 DELIVERIES OVER A NINE-YEAR PERIOD

A.

	BREECH PRESENTATION		CEPHALIC PRESENTATION		
	INFANT LIVED	INFANT DIED	INFANT LIVED	INFANT DIED	TOTAL
Spontaneous labor	5	3	8	7	23
Labor stimulated after spontaneous onset	2	1	1	4	8
Labor induced with Pituitrin	2	3	9	9	23
Total	9	7	18	20	54

B.

	NO. OF DELIVERIES	NO. OF CASES OF PROLAPSED CORD	INCIDENCE OF PROLAPSED CORD (%)
Spontaneous labor	15,940	31	0.195
Labor induced with Pituitrin	4,950	23	0.465
Total	20,890	54	0.258

Ruptures of the uterus (Table VII), excluding cases which did not occur primarily as a result of labor, numbered 8 in an eleven-year series of approximately 23,000 deliveries—an incidence of 0.035 per cent. The incidence in induced and spontaneous labors is essentially the same: 0.036 and 0.034 per cent.

TABLE VII. CASES OF RUPTURED UTERUS IN 23,000 DELIVERIES OVER AN ELEVEN-YEAR PERIOD

A.

	NO. OF CASES
Spontaneous labor	4
Labor stimulated after spontaneous onset	2
Labor induced with Pituitrin	2
Criminal abortion	1
Trial labor (spontaneous) after previous section	2
Term pregnancy after previous section (not in labor)	2
Total	13

B.

	NO. OF DELIVERIES	NO. OF CASES OF RUPTURED UTERUS	INCIDENCE OF RUPTURED UTERUS (%)
Spontaneous labor	17,520	6	0.0343
Labor induced with Pituitrin	5,450	2	0.0367
Total	22,970	8	0.0348

In part *B*, the incidences shown were calculated after cases associated with causes other than labor per se had been discarded. There is essentially no difference between induced and spontaneous labor.

Premature separation of the placenta (Table VIII), occurring after the onset of labor in pregnancies of thirty-six weeks or more, was recorded in 90 instances out of 23,091 deliveries over a ten-year period, with an incidence of 0.39 per cent. The incidence in induced labors (0.63 per cent) is significantly higher than in spontaneous labors (0.03 per cent).

TABLE VIII. CASES OF PREMATURE SEPARATION OF THE PLACENTA AFTER ONSET OF LABOR IN GESTATIONS OF 36 WEEKS OR MORE, IN 23,091 DELIVERIES OVER A TEN-YEAR PERIOD

A.

	NO. OF CASES
Spontaneous labor	46
Labor stimulated after spontaneous onset	12
Labor induced with Pituitrin	32
Total	90

B.

	NO. OF DELIVERIES	NO. OF CASES OF PREMATURE SEPARATION	INCIDENCE OF PREMATURE SEPARATIONS (%)
Spontaneous labor	18,039	58	0.0321
Labor induced with Pituitrin	5,052	32	0.633
Total	23,091	90	0.389

Cases were selected in which no causal factors other than labor per se were evident. Pituitrin induction is associated with a much higher incidence of this complication.

Laceration of the cervix extensive enough to cause excessive blood loss was recorded in 58 cases out of 11,359 deliveries, an incidence of 0.51 per cent. The incidence was 0.507 per cent in induced labors and 0.513 per cent in spontaneous labors (Table IX).

TABLE IX. CASES OF LACERATION OF THE CERVIX CAUSING EXCESSIVE BLEEDING IN 11,359 DELIVERIES OVER A FIVE-YEAR PERIOD

A.

	PRIMIGRAVIDAS	MULTIGRAVIDAS
Low Forceps.—		
Spontaneous onset of labor	8	9
Labor stimulated after spontaneous onset	6	1
Labor induced with Pituitrin	8	4
No Forceps.—		
Spontaneous onset of labor	2	8
Labor stimulated after spontaneous onset	0	3
Labor induced with Pituitrin	2	7

B.

	NO. OF DELIVERIES	NO. OF CASES OF LACERATION OF CERVIX	INCIDENCE OF LACERATIONS OF CERVIX (%)
Spontaneous labor	7,214	37	0.513
Labor induced with Pituitrin	4,145	21	0.507
Total	11,359	58	0.51

Cases were selected in which there was an estimated 500 c.c. or more blood lost, and which resulted in some signs of shock. There is no significant difference between induced and spontaneous labors, though the use of forceps does greatly increase the incidence.

Postpartum hemorrhage estimated to be of 500 c.c. or more, resulting in signs of shock, and of unspecified cause, was recorded in 75 cases out of 11,359 deliveries, with an incidence of 0.65 per cent. The incidence in induced labors was 0.76 per cent compared to 0.51 per cent in spontaneous labors (Table X).

TABLE X. CASES OF POSTPARTUM HEMORRHAGE OF 500 C.C. OR MORE, OF UNSPECIFIED CAUSE, IN 11,559 DELIVERIES OVER A FIVE-YEAR PERIOD

A.

	NO. OF CASES
Spontaneous labor	33
Labor stimulated after spontaneous onset	10
Labor induced with Pituitrin	32
Total	75

B.

	NO. OF DELIVERIES	NO. OF CASES OF POSTPARTUM HEMORRHAGE	INCIDENCE OF POSTPARTUM HEMORRHAGES (%)
Spontaneous labor	7,214	43	0.51
Labor induced with Pituitrin	4,145	32	0.76
Total	11,359	75	0.65

Primigravidas are compared in Table XI with multigravidas who develop these major complications for each of the three modes of labor. Table XII shows the percentage of primigravidas comprising the various groups as shown, the first column of figures giving the normal percentage of primigravidas for the periods studied. The complicated cases have a uniformly higher percentage of primigravidas with the exception of rupture of the uterus in which the percentage is zero. The highest percentage is in cases of laceration of the cervix where Pituitrin was used to stimulate labor.

TABLE XI. DIFFERENCES BETWEEN PRIMIGRAVIDAS AND MULTIGRAVIDAS IN OCCURRENCE OF 195 CASES OF RECORDED MAJOR COMPLICATIONS, REPRESENTING 23,091 DELIVERIES OVER A TEN-YEAR PERIOD

	ALL CASES		INDUCED LABOR		LABOR STIMULATED	
COMPLICATION	PRIMIGRAVIDA	MULTIGRAVIDA	PRIMIGRAVIDA	MULTIGRAVIDA	PRIMIGRAVIDA	MULTIGRAVIDA
Prolapsed cord (9 years)	24	30	11	12	2	6
Ruptured uterus (11 years)	0	8	0	2	0	2
Lacerated cervix (5 years)	26	32	10	11	6	4
Postpartum hemorrhage (5 years)	29	46	14	18	3	7
Total, all four complications	79	116	35	43	11	19

TABLE XII. PERCENTAGE OF PRIMIGRAVIDAS IN COMPLICATED AND UNCOMPLICATED CASES*

COMPLICATION	PRIMIGRAVIDAS IN ALL DELIVERIES DURING PERIOD OF STUDY (%)	PRIMIGRAVIDAS IN COMPLICATED CASES (%)		
		ALL MODES OF LABOR	INDUCED LABOR	PITUITRIN USED DURING LABOR
Prolapsed cord (1945 through 1953)	34	44	47.8	41.9
Ruptured uterus (1943 through 1953)	34.9	0	0	0
Lacerated cervix (1949 through 1953)	30.4	44.8	47.6	51.6
Postpartum hemorrhage (1949 through 1953)	30.4	38.7	43.7	40.5
Total, all four complications	—	40.5	44.9	42.6

*Based on cases shown in Tables VI, VII, IX, X, XI.

Postpartum inversion of the uterus has been recorded in only 3 cases in the past ten years. In all of these the clinical picture was unremarkable up to the time of its occurrence. No conclusions can be drawn from these few cases.

Comment

A number of considerations, not least of which are the personal qualifications of both patient and physician and the experience and quality of the nursing staff, must be weighed in judging whether elective induction is justified in an individual case. The factors of a patient leaving her home and family in good hands, who is then admitted in an orderly fashion without embarrassment or pain or uncertainty, who receives a good night's sleep before beginning a closely supervised labor, whose analgesia is ideal, whose delivery is certain to be attended, whose anesthetic is administered on an empty stomach, explain the popularity of the procedure.

Against this are an increased risk of premature separation of the placenta, and a slightly higher incidence of prolapsed cord and postpartum hemorrhage. Rupture of the uterus is a rare complication of labor except where section has previously been performed. When associated with Pituitrin, in our cases, it is parity of iv or greater that is the important factor, not excessive dosages. In only one case did stimulation with Pituitrin seem excessive and unwarranted. This was a 26-year-old gravida ii in whom a contraction ring developed prior to rupture. Prolonged labor was not a factor, duration ranging from two and one-fourth to ten hours and averaging six hours. There were no ruptures in primigravidas.

In the minds of a number of our staff, the important disadvantages of induction are: (1) the physician and the procedure are likely to be blamed, unjustifiably, for complications which arise subsequently; (2) routine induction on a large scale tends to lead to practices which by-pass the clinical judgment and experience that should be exercised in every case.

Certain criteria for induction are accepted by most authorities. Hanley[8] requires engagement of the presenting part, an adequate pelvis, and a cervix which is soft, 50 per cent or more effaced, and 1 to 2 cm. dilated. The presenting head in a multigravida may be riding out of the pelvis, yet engages with ease upon application of abdominal pressure or rupture of the membranes, and no difficulty ensues; or cervical effacement may not yet have occurred, yet the cervix shows excellent softening and dilatation, and induction proceeds with ease. In the occasional primigravida, the cervix is found far posterior and with no dilatation, but its soft consistency and good effacement enable safe induction with Pituitrin.

Cephalic presentation is not necessary. Stone and Tanz[4] in fact recommend the use of Pituitrin in breech presentation to shorten labor. Even an inadequate pelvis may not be an absolute deterrent; Lubin[5] recommends Pituitrin in cases of relative cephalopelvic disproportion. In addition to the usual criteria, it appears wise to include parity of iii or less where Pituitrin is to be used, amniotomy alone being safer and usually sufficient for patients of higher parity. Pituitrin should particularly be avoided when the uterus is overdistended by a large baby, twins, or polyhydramnios.

Erving and Kenwick[6] among other authors advise against elective induction in the case of primigravidas. The present study finds no ruptured uteri related to labor per se in primigravidas, but does disclose a higher incidence of certain other major complications, particularly where Pituitrin is used or labor is induced. Since the advantages of induction in preventing precipitate deliveries and unattended labors are largely nonexistent, it appears that primigravidity should weigh against elective induction though not necessarily contraindicate it. In these cases, cervical signs of inducibility of labor must be more strictly required, while multigravidas sometimes exhibit striking changes after a few contractions and descent of the fetal head.

Summary and Conclusions

1. An attempt has been made to describe the over-all picture of elective induction of labor as practiced in a private general hospital.

2. A survey of recent cases disclosed that labor was entirely spontaneous in 51.3 per cent of deliveries, induced in 32.2 per cent, and spontaneous in onset followed by stimulation with Pituitrin in 16.5 per cent.

3. The use of Pituitrin combined with amniotomy is eminently successful in producing labor.

4. The duration of labor, particularly the first stage, is shortened by the use of Pituitrin.

5. The incidence of underweight and premature infants is smaller in induced than in spontaneous labors.

6. The incidence of rupture of the uterus and significant laceration of the cervix is essentially the same in induced versus spontaneous labors.

7. The incidence of postpartum hemorrhage is slightly higher in induced labors.

8. The incidence of prolapse of the cord is higher in induced labor.

9. Premature separation of the placenta appears to occur much more frequently in induced labors.

10. The increase in the incidence of several infrequent complications of labor accompanying induction in the manner described must be weighed in the individual case against a number of real advantages, and the decision to perform induction made in the light of circumstances in which the procedure is done.

I wish to express my appreciation for the cooperation and kindness received from Dr. John Clancy, Chairman of the Department of Obstetrics, and from Sister Agnes of the Sacred Heart, Superior, Providence Hospital.

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INTRAVENOUS ETHYL ALCOHOL ANALGESIA WITH INTRAVENOUS PITOCIN INDUCTION OF LABOR

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NEEDLESS to say, the use of oral alcohol in medicine dates back to antiquity. The first available recorded use of alcohol for anesthesia, according to Keys,[1] dates back to 1513 when the fumes of alcohol were inhaled for anesthesic purposes. The failure of this method of anesthesia was soon apparent, and no further important use of alcohol in the anesthesic or analgesic field was reported until 1945 when Behan[2] reported, for the first time, the intravenous administration of ethyl alcohol as an analgesic agent in postoperative patients. Subsequently, there have been many reports in the literature on this subject,[3-7] and one of the latest by Karp and Sokal[8] reports its use over a nine-year period in two thousand patients. Thus, the postoperative use of intravenous ethyl alcohol as an analgesic has become an accepted procedure of proved worth.

A great deal of interest in intravenous alcohol was stimulated in 1929 by M. G. Marin[9] of Mexico City when he wrote his thesis, "Intravenous Anaesthesia With Ethyl Alcohol." Many subsequent reports appeared, most of which were derogatory. It must be pointed out, however, that there is a great deal of difference between the anesthesic and the analgesic dosage of alcohol. When it is used for anesthesia, the blood levels must be close to the lethal dosage; thus, its use for anesthesia has been condemned, and justifiably so. On the other hand, the blood levels that are necessary for analgesia are well within the limits of safety.

In 1950 Belinkoff and Hall[10] reported the first use of intravenous ethyl alcohol for analgesia during labor. They stated that very satisfactory analgesia was obtained without any harmful effects to either the mother or the baby. In 1951 Chapman[11] confirmed their findings and later[12] he stated that he was using intravenous ethyl alcohol exclusively, because of the lack of respiratory depression, for all patients in labor with premature babies. Fetchko and associates[13] used it for preinduction analgesia before starting inhalation anesthesia for delivery and were satisfied with the results. The latest report by Bourne, Roderick, and Philpott,[14] states that they found that the combined use of intravenous alcohol and intramuscular Demerol was a very satisfactory method of medication during labor.

From the pharmacological point of view, alcohol is an excellent drug to use during labor. It is a sedative, analgesic, hypnotic, euphoric, vasodilatory, caloric, and antipyretic drug. In obstetrics our main concern with its pharmacology centers around the analgesic, sedative, and hypnotic reactions. It has been well established that alcohol has a sedative effect on the higher centers

of the central nervous system, which is desirable. What is even more important is that it is a central nervous system respiratory stimulant.[15] Thus, we have a drug that has many advantages in obstetrics. Because of the metabolism of alcohol in the liver, it is probably not wise to use it in patients with toxemia or demonstrable liver disease. It is also contraindicated in epileptics.

Since 1948, when Theobald and associates[16] reported the induction of labor with the use of drip intravenous Pitocin, there has been much interest in the subject. Its usefulness and limitations have been well established and well summarized by Page.[17] One of the disadvantages of the use of alcohol is the necessity of its administration by the intravenous route. It occurred to me that if an induction of labor was being done with intravenous Pitocin, then the administration of ethyl alcohol by the same needle would be a simple and effective method of giving a safe analgesic with no additional nursing care necessary. Since my preliminary report[18] on the combined use of intravenous ethyl alcohol and Pitocin, I have used this method on an additional 250 patients, and have found it a most satisfactory method of induction and analgesia.

Materials

The solution of Pitocin consisted of 5 oxytoxic units of Pitocin added to 1,000 c.c. of 5 per cent dextrose in distilled water. When analgesia was needed, the 7½ per cent solution of ethyl alcohol was started by inserting the needle of this solution into the tubing of the Pitocin that was already running into the vein. The 7½ per cent alcohol solution was made by removing 90 c.c. of fluid from a 1,000 c.c. bottle of 5 per cent dextrose in distilled water, and then adding 90 c.c. of 95 per cent ethyl alcohol. As the 95 per cent ethyl alcohol is a sterile solution,[6] it may be used just as it comes from the pharmacy. Thus, these solutions are easily prepared by the nurse from materials that are readily available in any hospital.

Procedure

All of the inductions were of the "routine and convenience" type. No inductions for medical reasons were included in this report so that the results would not be confused with other obstetrical complications. Contraindications to inductions included cephalopelvic disproportion, grand multiparity, toxemias, abnormal presentations, vaginal bleeding, and placental separation.

Patients were admitted to the hospital at term when the presenting part was well engaged, the cervix was 50 per cent effaced, and the cervix was 1 to 2 cm. dilated. After a routine preparation and enema, the Pitocin was started. The solutions were given into an antecubital or forearm vein. The Pitocin was given at a rate of 10 to 20 drops per minute or was regulated by the response of the uterus. This was continued until almost full cervical dilatation and then stopped. The intravenous alcohol was started as soon as the patient requested medication, for patients were told that they might have medication as early as they desired it. When a short labor was expected, the alcohol was started either before or simultaneously with the Pitocin.

The alcohol was continued until the anesthesia for the delivery was given. Low spinal anesthesia was used for 95 per cent of the deliveries, and nitrous oxide and/or ether in the remainder. The alcohol was started as rapidly as it would run in, until 150 to 200 c.c. had been given, then the rate was slowed

to 60 to 80 drops per minute. The average adult can metabolize 10 c.c. of pure ethyl alcohol per hour[15] or 150 c.c. of a 7½ per cent solution. Thus, 150 c.c. per hour of the alcohol solution is a minimal amount once a blood level has been obtained. The first sign that an excessive amount of alcohol has been given is nausea, followed in a few minutes by vomiting. When either is noted, the alcohol solution has only to be slowed in rate for 5 to 10 minutes, but it is not necessary to stop it. After the nausea has ceased, the rate may then be increased again. A 7½ per cent solution of alcohol was found to be the most satisfactory concentration, although some authors prefer a 5 per cent solution.

In some cases not included in this report, attempts were made to combine the two solutions into one bottle, but it was impossible to find a ratio of Pitocin and alcohol that would be satisfactory for any two patients. The regulation of the rate of flow of the alcohol by the response of the patient was easily mastered by the obstetrical nurses in a short period of time. There were no local reactions to the alcohol at the site of the needle even when the needle slipped out of the vein by error and the solutions went into the subcuticular tissues. Demerol and scopolamine were given as indicated by the reaction of the patient, or on request of the patient. No barbiturates were given because they were previously found to be completely unnecessary. The membranes were ruptured artificially in 83 per cent of the cases, as soon as the patient was in good active labor. In the rest of the cases the membranes either ruptured spontaneously or labor progressed so rapidly that it was not necessary to rupture them.

Results

This method of induction and sedation was used on 250 patients. No adverse effects from the alcohol or the alcohol-Pitocin combination were noted. The results with respect to the quantities of solution, medications, and the duration of labor are given in Table I. It will be noted that the labors were relatively short and the amounts of Demerol and scopolamine were about one-fourth to one-half those that were previously given prior to the use of alcohol. As previously stated, no barbiturates were given. The analgesic effect on the patient was found to be directly proportionate to the amount of alcohol and Demerol given. The amnesic effect was proportionate to the amount of scopolamine given. The subjective reactions of the patients to the intravenous alcohol were very interesting to watch. It was found that the best analgesic effect was obtained when the patient did not know that she was receiving alcohol. In the few patients who inadvertently discovered that they were getting alcohol, it had the usual reaction that one would expect after a few cocktails. The other patients had a conscious euphoria during a pain and then were sleepy in between pains. No excitement reactions were seen. There were no sequelae in the postpartum period. One does not encounter a "hangover" from the administration of chemically pure ethyl alcohol by the intravenous route, as with the ingestion of alcohol in beverage form.

With one exception, all the patients were well pleased with the medication during labor. All of the multiparous patients considered it the easiest labor that they had had. All of the 250 patients went into immediate effective labor and progressed in a rapid and normal fashion. All of the deliveries were spontaneous or by outlet forceps. There were no delays in the third stage of labor and the total blood loss was within normal limits.

No depression of the babies was noted. All of the babies cried spontaneously without any resuscitation being necessary. Work done by previous authors[10, 13] shows that the blood levels of alcohol of the babies at birth are 20 per cent to 50 per cent lower than those of the mothers, thus indicating that

the alcohol crosses the placental barrier easily. But this is of little importance because the alcohol is metabolized rapidly and also because it is not a respiratory depressant.

TABLE I

DURATION OF LABOR (HOURS)		ALCOHOL 7½% (C.C.)	PITOCIN 5 UNITS/ 1,000 C.C. (C.C.)	DEMEROL (MG.)	SCOPOLAMINE (MG.)
PRIMIPARAS	MULTIPARAS				
6.8	4.7	718	414	130	0.6

Conclusions

1. There were no contraindications found to the combined use of intravenous ethyl alcohol and intravenous Pitocin.

2. When the intravenous Pitocin is being used, there is no inconvenience in using intravenous alcohol at the same time.

3. Patients require a minimal amount of watching during labor because any excessive amount of alcohol is easily noted and controlled.

4. The effect of the intravenous Pitocin and the conduct of the labor and delivery were not affected by the intravenous alcohol.

5. Very minimal amounts of Demerol and scopolamine were necessary to produce deep sedation and amnesia for the mother.

6. All of the babies cried spontaneously and showed no evidence of respiratory depression.

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7 HYDE AVENUE

NUTRITION STUDIES OF PREGNANT AUSTRALIAN WOMEN*†

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PART I. MATERNAL NUTRITION IN RELATION TO TOXEMIA OF PREGNANCY AND PHYSICAL CONDITION OF INFANT AT BIRTH

MANY studies have indicated an association of maternal nutrition with growth and development of the fetus, prematurity, stillbirth and neonatal death, with toxemia of pregnancy, and with lactation; other studies have failed to demonstrate such a relationship.[1, 2,a, 3, 4] Difficulty in obtaining experimental situations that are comparable or where maternal diet is the only variable may explain seemingly contradictory results. If diet is to be related to the outcome of pregnancy and the results of various projects compared, appreciation of the time factor in nutritional studies[5] and of methods of dietary data collection and rating is of utmost importance in the interpretation of findings.

The present study was designed to investigate the influence of maternal diet on, and its relation to, the course and outcome of pregnancy and to incidence, and duration of lactation in a group of Australian women. The findings will be viewed especially in relation to the studies of Hamlin[6] and of the National Health and Medical Research Council[7] on groups of Australian women and also in relation to the Harvard Studies.[8, 9]

Hamlin reported results of a four-year anti-eclampsia campaign conducted at the Women's Hospital, Sydney, Australia, in which during the last year of the campaign eclampsia was eliminated and the incidence of pre-eclampsia reduced among "booked" patients (5,000 in number). Seven steps, including lectures on diet and control of weight gain in mid-pregnancy by dieting, were described and considered responsible for the success of the campaign. No quantitative data were compiled on dietary intakes.

The National Health and Medical Research Council of Australia in their inquiry into the medical aspects of the decline of the birth rate made "an investigation into the effects of nutrition upon the course and outcome of pregnancy" among 406 pregnant women drawn from lower economic sections of and attending prenatal clinics in Sydney and Melbourne, Australia. They used a "personal interview" method for collection of dietary data. The levels of

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consumption by each patient of the four nutrients: protein, calcium, vitamin B_1 and vitamin C (''the nutrients most likely to be inadequate in the average Australian diet'') were used to rate the diets. Patients were accordingly divided into three groups: a ''good'' diet group, an ''inadequate'' diet group and an ''indeterminate'' group.

In the Harvard Study of 216 pregnant women, largely of Northern European stock of ''middle class'' economy, chosen from the prenatal clinics of the Boston Lying-in Hospital, the Burke Research Dietary History Method[10] was used for collection of dietary data. For evaluating these data a five-point rating scale (''excellent,'' ''good,'' ''fair,'' ''poor,'' and ''very poor'') was used in this study for each essential nutrient, based upon comparison with an arbitrary set of values (approximating the values recommended by the Food and Nutrition Board of the National Research Council) accepted as optimum. These same methods of collection and rating of dietary data were used in the present study.

Selection of Groups and Methods

The subjects, 52 primiparas and 134 multiparas attending the antenatal clinic of the King George V Memorial Hospital for Mothers and Babies in Sydney, Australia, were selected for interview on the basis of obstetrical examination that gave no indication of abnormality. A history of previous toxemia of pregnancy was not cause for exclusion, but more than one previous miscarriage or stillbirth excluded a subject from the study. A research dietary history that was reasonably reliable was a requirement. The study was conducted during the years 1948-1950.

The study group was racially homogeneous, all subjects were born in the State of New South Wales and the group was typical of the Australian population of the day. The subjects were young mothers, 136 were under 30 years of age, and the multiparas were mothers of small families. They were not from the poorest economic group in Sydney: 91 per cent of the husbands earned more than the current basic minimum wage.

The toxemia and prematurity data were taken from hospital records and may not be as accurate as data collected in a research study.

Patients who were admitted to the King George Hospital from the antenatal clinic on the diagnosis of toxemia by staff obstetricians furnished the cases of toxemia in the study. The diagnosis was based on the standard set by Mayes* (1950). Two categories of toxemia were included:

(A) A rise in blood pressure associated with albuminuria.

(B) A rise in blood pressure combined with a clinical diagnosis of toxaemia based on the presence of oedema, excessive and sudden weight gain.

The case records which fell into category B were reviewed by Professor Mayes before being classified as toxemia for this study.

The standard for prematurity was that suggested by Potter[11] and reads as follows:

A baby is called premature if two of the following are satisfied:

(1) Thirty-eight weeks gestation or under;

(2) A birth weight of 5 lbs. 8 oz. or under; and

(3) A crown-heel length of 18 inches or under.

*Professor Bruce T. Mayes is the Head of the Department of Obstetrics at the University of Sydney, Sydney, Australia.

A case was classified as an abortion if the subject miscarried before the twenty-eighth week of gestation.

The state (New South Wales) statistician's official definitions[12] were used as standards for stillbirths and neonatal deaths:

> A still born child is one of seven months gestation or over, not born alive and which measures at least fourteen inches but does not include any child which has actually breathed.
>
> A neonatal death is a death of a live born child within one week of birth.

Dietary data were obtained for three periods: previous to pregnancy, first half of pregnancy, and second half of pregnancy. The food pattern of Australians is relatively simple and stereotyped. Nevertheless, it was felt that the nutritional data obtained from the subjects did not justify interpretation for the individual and therefore were used only for comparison on a group basis. Details of collection, analysis, and ratings of diets have been previously reported.[13]

Results and Comment

Toxemia.—

Incidence.—In this study there was a 14.0 per cent incidence of toxemia (26 cases among 186 pregnancies). In King George V Hospital from which the subjects were drawn there was an 11.6 per cent incidence for the year July, 1949, to June, 1950. The difference in incidence between the study group and the total hospital statistics was not significant even though the hospital figures also included patients from higher economic groups than that of which the study group was composed.

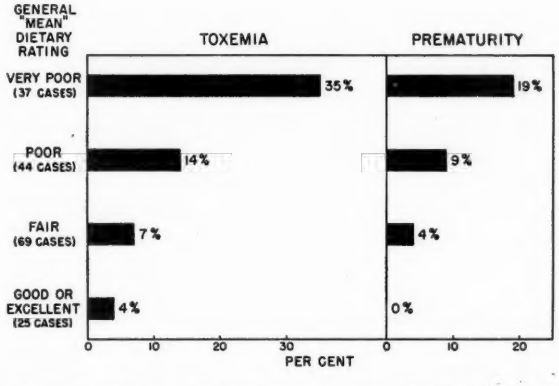

Fig. 1.—Maternal diets in the latter half of pregnancy related to toxemia and prematurity.

The incidence of toxemia varies throughout the world from 0 to 28 per cent.[14] In many areas the incidence has decreased in recent years. However, it still remains one of the leading causes of maternal deaths. The incidence of toxemia among 216 pregnant women in the Harvard Study was 12.9 per cent and in the Australian National Health and Medical Research Study there was an 8.6 per cent incidence.

Incidence in Relation to Maternal Diet.—In the present study the incidence of toxemia in relation to over-all maternal diet was 42.1 per cent in the "very poor," 21.2 per cent in the "poor," 9.7 per cent in the "fair," 7 per cent in the "good," and 5.6 per cent in the "excellent" diet groups. Table I gives the incidence of toxemia related to maternal diet previous to pregnancy, during the first and during the second half of pregnancy, and to over-all dietary ratings.

The relationships in all four periods have a high statistical significance. Fig. 1 demonstrates graphically the relation found in this study between maternal diet during the latter part of pregnancy and both toxemia and prematurity.

TABLE I. TOXEMIA RELATED TO MATERNAL DIET

GENERAL "MEAN" RATING OF MATERNAL DIETS	MATERNAL DIET PREVIOUS TO PREGNANCY			MATERNAL DIET IN FIRST HALF OF PREGNANCY			MATERNAL DIET IN SECOND HALF OF PREGNANCY			MATERNAL DIET IN PREGNANCY, TOTAL (AVERAGE)		
	TOTAL NO. CASES	TOXEMIA NO. OF CASES	TOXEMIA %	TOTAL NO. CASES	TOXEMIA NO. OF CASES	TOXEMIA %	TOTAL NO. CASES	TOXEMIA NO. OF CASES	TOXEMIA %	TOTAL NO. CASES	TOXEMIA NO. OF CASES	TOXEMIA %
Indefinite*	11	1		11	1		11	1		11	1	
Very poor	27	10	37.0	9	5	55.6	37	13	35.1	19	8	42.1
Poor	42	7	16.7	22	7	31.5	44	6	13.6	33	7	21.2
Fair	76	4	5.3	49	6	12.2	69	5	7.2	62	6	9.7
Good	15	4	26.7	28	4	14.3	17	1	5.9	43	3	7.0
Excellent	15	0	0	67	3	4.5	8	0	0	18	1	5.6
Total	186	26		186	26		186	26		186	26	
	P = 0.011			P = 0.001			P = 0.016			P = 0.010		

P in each period is highly significant

*This class contains patients who aborted or vomited, making it impossible to calculate all three periods; this class was excluded when testing for statistical significance.

Several researchers have suggested a relationship between maternal diet and the development of toxemia. In the Harvard Study there was a 44 per cent incidence of toxemia among the women whose diets were rated as "poor to very poor" and an 8 per cent incidence among the women with "fair" diets, while no toxemia occurred among the women with "good" or "excellent" diets. The relationship was statistically significant. In the Australian National Health and Medical Research Council Study, among the women with a "good" diet the incidence of toxemia was 4.9 per cent; among the "inadequate" diet group there was a 14.5 per cent incidence. Burke and Kirkwood,[15] in a preliminary report of effects of nutrition consultation services to patients in the Toxemia Clinic of the Boston Lying-in Hospital, concluded that in the prevention and treatment of toxemia control of the nutritional state of the woman appeared to be an important factor in relation to the prevention and treatment of toxemia. The diets used in the clinic were high protein, controlled at a normal or slightly lower caloric level, and the sodium content was restricted as seemed necessary. Hamlin also considered dietary improvement, effected by group education and by individual instruction, one of the most important of the several steps responsible for the elimination of eclampsia in the Women's Hospital, Sydney. In sharp contrast to these findings, Smith[5] found that toxemia was not increased during the 1944-1945 hunger period in Holland but by certain criteria was actually decreased in comparison with expected frequency. Smith discussed the possible explanation of the striking difference between his findings and those of other workers; he believed that the most likely interpretation of the controversial evidence was that the nutritional circumstances were not comparable; acute undernutrition such as that of the Dutch women might result in one way while chronic undernutrition might result in another.

Incidence Related to Parity.—For this study, Table II shows the incidence of toxemia related to parity. Among the 52 primiparas 28.8 per cent had toxemia, while in the 134 multiparas the incidence was 8.2 per cent, a difference demonstrated to be significant. It is well known that toxemia is much more common among young primigravid than in older and multiparous women. In the National Health and Medical Research Council's Study the incidence of toxemia was significantly higher in primiparas than in the multiparas. In the

study at the Women's Hospital, Sydney, it also was found "that the women who were troubling the hospital most with rapidly progressive grave pre-eclampsia were the young primiparae."

TABLE II. INCIDENCE OF TOXEMIA IN RELATION TO PARITY

	PARITY						TOTAL MULTIPARAS	TOTAL
	i	ii	iii	iv	v	v+		
Number of cases	52	65	33	25	8	3	134	186
Incidence of toxemia	15	7	3	1	0	0	11	26
% Incidence	28.8	10.8	9.1	4	0	0	8.2	14.0

P = Less than 0.01

Incidence in Different Diet Groups With Respect to Parity.—Table III shows the incidence of toxemia in this study in the different diet groups with respect to parity. Among the multiparous patients the distribution of toxemia among the different diet groups in the two periods, previous to pregnancy and second half of pregnancy, indicate a relationship between "poor" diets and toxemia. The relationship, however, is not apparent among the primiparous patients nor during the first half of pregnancy among the multiparas. There were too few cases of toxemia to test the significance of this apparently different relationship. It could not be ascribed, however, to difference in food habits between primiparas and multiparas, as no statistical difference was found between the number of toxemia cases in each of the six diet groups.

In the National Health and Medical Research Council Study it was found that among the multiparous patients there was a significant difference, due to diet, in the incidence of toxemia, with a higher incidence in the "unsatisfactory" diet group, while among the primiparous patients this difference was apparent in the Melbourne series but not in the Sydney series.

Incidence Related to Pregravid Weight and Weight Gain During Pregnancy.—Table IV shows the incidence of toxemia among the 31 overweight* (pertaining to weight prior to pregnancy) subjects of this study as compared with others in the group. A statistically significant association was found between prepregnancy obesity and incidence of toxemia. However, such relationship could not be demonstrated between excessive weight gain during pregnancy (35 pounds or more or 30 per cent or more over weight prior to pregnancy) and the incidence of toxemia.

Chesley[17] has made an extensive study of weight changes in pregnancy and states that the average weight gain based on reports in the literature is 24.0 pounds (10.9 kilograms). Excessive weight gain has been associated with toxemia. On the other hand "every patient whose total weight gain is over 10.9 kilograms does not necessarily have toxemia. Statistics do show, however, that the incidence of toxemia is increased in those patients who gain more than 13 kilograms (28.7 lbs.). The total gain in pregnancy is not so important as the rate of gain. Patients who gain more than 0.6 kilograms (1.3 pounds) per week have an increased incidence of toxemia, especially pre-eclampsia."[14] Hamlin states that in his experience "almost every young primipara destined to have pre-eclampsia or eclampsia in the last ten weeks of pregnancy has, between the twentieth and thirtieth weeks, given a clear warning of the destiny which awaited her. This warning is the record of her weight during these important weeks." The experience of the Harvard Group working in the toxemia clinic of the Boston Lying-in Hospital is in agreement with these findings (unpublished results).

*An overweight subject was one who was 2 standard deviations or more above the mean weight for specific age and height. The standard of weight for height and age of Australian women used has previously been described.[16]

TABLE III. TOXEMIA RELATED TO MATERNAL DIET AND PARITY

GENERAL "MEAN" RATING OF MATERNAL DIET	MATERNAL DIET PREVIOUS TO PREGNANCY				MATERNAL DIET IN FIRST HALF OF PREGNANCY				MATERNAL DIET IN SECOND HALF OF PREGNANCY			
	PRIMIPARAS		MULTIPARAS		PRIMIPARAS		MULTIPARAS		PRIMIPARAS		MULTIPARAS	
	TOTAL NO. CASES	TOXEMIA NO. CASES	TOTAL NO. CASES	TOXEMIA NO. CASES	TOTAL NO. CASES	TOXEMIA NO. CASES	TOTAL NO. CASES	TOXEMIA NO. CASES	TOTAL NO. CASES	TOXEMIA NO. CASES	TOTAL NO. CASES	TOXEMIA NO. CASES
Indefinite	2	1	9	0	2	1	9	0	2	1	9	0
Very poor	10	4	17	6	2	1	7	4	10	6	27	7
Poor	13	5	29	2	7	5	15	2	17	4	27	2
Fair	19	1	57	3	18	3	31	3	16	3	53	2
Good	4	4	11	0	10	4	18	0	4	1	13	0
Excellent	4	0	11	0	13	1	54	2	3	0	5	0
Total	52	15	134	11	52	15	134	11	52	15	134	11

Differences in dietary ratings between multiparas and primiparas were tested and found *not* statistically significant.

TABLE IV. INCIDENCE OF TOXEMIA AND PREMATURITY IN SUBJECTS WITH PRECONCEPTIONAL OBESITY*

	NO. OF CASES	TOXEMIA†		PREMATURITY‡	
		INCIDENCE	%	INCIDENCE	%
Cases of obesity	31	8	25.8	2	6.4
Other cases	152	18	11.8	13	8.3
Cases with no weight data	3	0		0	
Total	186	26	13.9	15	8.06

*Obesity is defined as plus 2 standard deviations or more above the mean for specific age and height (Australian standard, Woodhill[16]).

†P=0.039.

‡Relationship not significant.

The etiological agent causing toxemia of pregnancy is not known. It does appear, however, that there is a relationship between toxemia and maternal diet and that control of the nutritional state of the pregnant woman is an important factor in relation to the prevention and treatment of toxemia.

Prematurity.—

In this study there were 15 premature infants. The distribution of these infants among the different diet groups is shown in Table IV. With respect to diet previous to pregnancy, no statistically significant relationship could be demonstrated between diet and incidence of prematurity. For the first half of pregnancy a relationship significant at the 6 per cent level was shown, and for the second half of pregnancy a relationship significant at the 1 per cent level. The relationship for the latter half of pregnancy is shown graphically in Fig. 1.

In view of the uncertainty about when increased requirements for nutrients in pregnancy should be allowed to affect dietary ratings, this difference in relationship of prematurity to the different periods of pregnancy does not necessarily mean that there is a more direct relationship between diet and prematurity in the latter half of pregnancy than in the first half. This may simply mean that because of the capacity of the pregnant woman to store nutrients, the increased dietary allowances for the latter part of pregnancy should be used for rating diets also at the beginning of pregnancy. On the other hand, it is well known that during the second half of pregnancy the fetus draws heavily on the mother for protein and calcium, two nutrients which would affect the birth weight and birth length of the baby, i.e., two of the criteria upon which the standard for prematurity is based.

TABLE V. MEAN BIRTH LENGTHS OF BABIES RELATED TO MATERNAL DIET

MATERNAL DIET PREVIOUS TO PREGNANCY					MATERNAL DIET, TOTAL PREGNANCY (AVERAGE FIRST AND SECOND HALVES)				
GENERAL "MEAN" RATING OF MATERNAL DIETS	BIRTH LENGTHS OF BABIES				GENERAL "MEAN" RATING OF MATERNAL DIET	BIRTH LENGTHS OF BABIES			
	MEANS		STANDARD DEVIATIONS			MEANS		STANDARD DEVIATIONS	
	INCHES	CM.	INCHES	CM.		INCHES	CM.	INCHES	CM.
Poor and very poor (74 cases)	*20.85	52.95	1.21	3.02	Poor and very poor (53 cases)	†21.02	53.35	1.00	2.50
Fair (76 cases)	21.19	53.85	1.04	2.60	Fair (61 cases)	21.22	53.92	1.08	2.70
Good and excellent (31 cases)	*21.71	55.10	0.25	0.62	Good and excellent (60 cases)	†21.39	54.35	0.87	2.18
Total cases 181‡					Total cases 174§				

*Difference statistically signficant (P=less than 0.0001).

†Difference statistically significant (P=0.04).

‡Four patients aborted, 1 case record incomplete for birth length.

§Four patients aborted, 7 vomited during pregnancy and so prevented dietary rating, 1 case record incomplete.

TABLE VI. MEAN BIRTH WEIGHTS OF BABIES RELATED TO MATERNAL DIET

MATERNAL DIET PREVIOUS TO PREGNANCY							MATERNAL DIET TOTAL PREGNANCY (AVERAGE FIRST AND SECOND HALVES)						
GENERAL "MEAN" RATING OF MATERNAL DIETS	BIRTH WEIGHTS OF BABIES						GENERAL "MEAN" RATING OF MATERNAL DIETS	BIRTH WEIGHTS OF BABIES					
	MEANS			STANDARD DEVIATION				MEANS			STANDARD DEVIATION		
	POUNDS	OUNCES	KILOGRAMS	POUNDS	OUNCES	KILOGRAMS		POUNDS	OUNCES	KILOGRAMS	POUNDS	OUNCES	KILOGRAMS
Poor and very poor (74 cases)	*7	1.19	3.22	1	2.7	.51	Poor and very poor (53 cases)	†7	0.30	3.19	1	2.33	.52
Fair (76 cases)	7	6.86	3.38	1	1.31	.49	Fair (61 cases)	7	1.57	3.23	1	2.02	.51
Good and excellent (31 cases)	*7	11.35	3.50	0	11.45	.32	Good and excellent (60 cases)	†7	11.27	3.50	0	12.15	.34
Total 181 cases‡							Total 174 cases§						

*Difference statistically significant (P=0.0028).
†Difference statistically significant (P=0.0002).
‡Four patients aborted, 1 case record incomplete for birth length.
§Four patients aborted, 7 vomited during pregnancy and so prevented dietary rating, 1 case record incomplete.

Tables V and VI show the mean birth length and mean birth weight of the babies (including 2 stillborn infants) in the study. Because of the small number of premature babies the diets were grouped with respect to 3 major diet groupings: "excellent to good," "fair," and "poor to very poor" (to allow for statistical study of the data), for two periods, previous to and during pregnancy. The figures on birth lengths and on birth weights indicate that there is an over-all relationship between the diet of the mother and the size of the infant.

The results on birth lengths and birth weights are in agreement with those of Burke and associates where babies were accurately measured and weighed and they seem further to substantiate evidence of the role of maternal nutrition as one of the factors which may be related to prematurity (size of infant).

Burke and co-workers found that all but one of the premature infants (under 5 pounds at birth) and all of the infants considered "functionally immature" were born to mothers in the "poorest" diet group. The average birth weight of infants born to mothers in the "excellent or good" diet group was 8 pounds 8 ounces, in the "fair" diet group 7 pounds 7 ounces, and in the "poor to very poor" diet group 5 pounds 13 ounces. The average lengths were respectively 51.8, 50.0, and 47.2 cm.; these length-diet relationships give added importance to the weight-diet relationships as birth length is one of the criteria often used for standards upon which prematurity is based. Antonov[18] describes the children born during the siege of Leningrad, 1942. He classed as immature those infants "less than 47 cm. long at birth" and on that basis found that the rate of prematurity among infants conceived just previous to a period of acute hunger rose to the unusually high figure of 41.2 per cent during the first half of that year. The number of children with low birth weights was also striking; of those born in the first half of 1942, 49.1 per cent weighed less than 2,500 grams and only 4 per cent weighed more than 3,500 grams. In the National Health and Medical Research Council Study, on the other hand, the workers could find no statistically significant difference in the incidence of prematurity (based on standards of Potter, referred to before) between a "good" and an "inadequate" diet group; they conclude that the degree of adequacy of the maternal diet did not influence the birth weight of the baby. Smith[19] studied the effects of wartime starvation upon the size of the newborn infant in Holland. He analyzed infant birth weights and lengths not in the conventional way of average figures, but on a percentile basis. He found a decline in weight at all percentiles, the amount representing between 8 and 9 per cent of the weight in normal times, the percentage being only slightly greater in the ninetieth percentile than in the tenth percentile group. Smith states that the "entire phenomenon of weight decline though of statistical significance was apparent only when infants were analyzed by groups"; that "the return of food was reflected by an increase in birth weight in a manner indicating that fetal weight gain is particularly related to the diet of the last half or last trimester of pregnancy." A significant decline in birth length, though less clearly apparent than the change in weight, also occurred, while prematurity based on a weight criterion (5 pounds or under) alone and for the group as a whole was only insignificantly increased. This seeming inconsistency again calls attention to the difficult question of how prematurity is to be identified. Dean[3] points to the limitations of the criteria of size often used in defining prematurity for lack of anything better. He discusses factors which might affect the size of the infant, sometimes through influences on the duration of pregnancy. He also warns against the practice of relying on crude average weight and length figures which might be misleading and might account for discrepancies found in reports dealing with birth weights and lengths of infants.

In an analysis of the records of 22,000 births at the Landesfrauenklinik Wuppertal, during the years 1937 to 1948, data for birth weight and length

were grouped and studied with consideration of factors associated with the size of the newborn.[3] The results complemented those of Smith, the average birth weight was lowest in 1945, the year in which there was probably the greatest shortage of food. There was also a reduction in length and the period of gestation was slightly shortened, though not enough to account for the reduction in weight.

Of special interest in this connection are the studies of Wallace[20] upon maternal undernutrition during late pregnancy in sheep where weights of newborn lambs were markedly reduced, also lengths to some extent.

Abortions, Stillbirths, Neonatal Deaths, and Congenital Defects.—

The National Health and Medical Research Council state that from their results "it is reasonable to conclude that the prenatal level of nutrition of Australian women at the time of [their] survey was not an important factor in predisposing towards stillbirths, neonatal death and foetal abnormalities." It was pointed out, however, that there were very few cases upon which to base this statement. In the 216 cases studied by Burke and her associates, every stillborn infant, every infant who died within a few days of birth except one, and the majority of infants with marked congenital defects were born to mothers in the poorest diet group—showing a significant relationship between prenatal diet and the condition of the infant at birth. Smith,[5] on the other hand, found that in Holland during the 1944-1945 winter no effect of maternal undernutrition was noted upon the incidence of stillbirths or neonatal deaths and that congenital malformations were slightly but not significantly increased; the sharp fall in conception rate associated with amenorrhea resulted in so few pregnancies that data were inconclusive as to the relation of malformation of the fetus and undernutrition in early pregnancy, i.e., the period implied by Warkany[21] in which maternal malnutrition in animals might result in fetal maldevelopment. Figures for abortion and miscarriage were included in Smith's report but because these statistics were unreliable no attempt was made to draw conclusions from them.

In the present series there were 4 abortions, 2 stillbirths, 4 neonatal deaths, and 8 congenital defects. No case of abortion or neonatal death occurred in either the "good" or the "excellent" diet groups, there was one stillbirth in the "good" diet group but only with respect to diet during the first half of pregnancy. Of the congenital defects in relation to over-all average maternal dietary ratings, one case appeared in the "good" diet group; with respect to maternal diet rating for the first half of pregnancy there was one in the "good" and one in the "excellent" diet group; but with respect to the second half of pregnancy and to dietary ratings of the period previous to pregnancy, there were no congenital defects in either the "excellent" or the "good" diet group. Here again the arbitrary difference between dietary ratings of the first and latter halves of pregnancy might explain this different relationship. On the other hand, the influence of the time factor in nutritional relationships has been exhibited in animal experimentation. Pertinent animal experiments with regard to manifestations of prenatal nutritional deficiency, many of which were initiated by an interest in dietary effects on the outcome of pregnancy in human beings, have been summarized by Warkany.[21]

The results of this study seem further to confirm previous evidence, accumulated in human as well as animal research, of the importance of prenatal nutrition to the growth and development of the fetus.

Summary

The results of a study intended to evaluate the maternal-fetal aspects of nutrition in a group of 186 pregnant Australian women have been presented.

A statistically significant relationship was demonstrated between poor maternal diets and the incidence of toxemia and of prematurity. Toxemia also was shown to be associated with prepregnancy obesity, though not with excessive weight gain during pregnancy.

No conclusions could be drawn with regard to the level of nutrition and frequency of abortions, stillbirths, neonatal deaths, or congenital defects, the occurrences in this sample being too small to allow for statistical interpretation.

PART II. MATERNAL DIET AND THE DURATION OF LACTATION

Reports in the literature have implicated nutrition as a factor affecting the ability of a mother to breast feed her child. Many of these reports, however, have expressed opinions with little factual evidence.

All attempts to confirm a suggestive relationship between maternal nutrition and lactation have to contend with the prevailing wide variation in the incidence of breast feeding. In times past it was the natural and accepted procedure for a mother to nurse her infant but today the custom of breast feeding varies widely in different countries,[7, 22, 23, 24, 25] within the same country,[24] even within the same environment.[26] Breast feeding is easily influenced by cultural, psychological, and physical factors, and situations where maternal diet is the only variable are rare, if not nonexistent.

One method of securing data which might help clarify the relationship of maternal nutritional status with ability to lactate is to study the effect of wartime deprivation on the incidence and duration of lactation.[3, 18, 19] A second way is comparison of data on lactation of a group of women with "improved" nutrition with that of a control group.[27] A third method is to analyze the diets of mothers living in an area where breast feeding is widely accepted[7] with the subsequent comparison of the level of nutrition and the ability to lactate. An area where the incidence of breast feeding is high provides a situation where sociological and psychological variables affecting lactation are, while not eliminated, minimized.

The material presented here deals with prenatal dietary and lactation information obtained by the senior author of this paper from a group of Australian women, drawn from the antenatal clinic of the King George V Memorial Hospital for Mothers and Babies and described in Part I. The impression of the senior author is that in Australia the incidence of breast feeding is relatively high. A study by the National Health and Medical Research Council[7] of the adequacy of lactation in a group of mothers in Sydney, Australia, lends support to this view.

Methods of dietary data collection, analysis, and rating employed in this study have been reported.[13] Data on lactation were obtained from 159 of the 186 study cases by means of mail questionnaires. It was necessary to complete the investigation when some of the babies were only 5 months old. Therefore the lactation information up to the fifth month is based on 159 cases, while that with respect to the seventh month is based on 138 cases. The women at the time of discharge from the hospital were advised of the questionnaires they would

receive. The questionnaire was intended to furnish information on duration of complete breast feeding.* The return of completed forms proved very satisfactory (Table VII).

TABLE VII. DATA ON LACTATION

	NO. OF CASES
Cases with data to the end of the lactation period	131
Additional cases with data to at least the fifth month of lactation	21
Cases with vomiting during pregnancy, making diet classification impossible	7
Abortions, stillbirths, and neonatal deaths	10
Cases with no lactation data	17
Total	186

The study reports the incidence of complete breast feeding through the first, third, fifth, and seventh months, respectively, and relates the duration of lactation to the maternal dietary intakes during pregnancy. No data were collected on the mother's ability to breast feed, the establishment of lactation, the incidence of lactation at the time of discharge from the hospital, or the diet of the lactating mother.

Results and Comment

Incidence.—Fig. 2 shows graphically the incidence of complete breast feeding in this study at various periods of lactation. Eighty per cent of the infants were completely breast fed through the first month of life, and 63, 49, and 30 per cent through the third, fifth, and seventh months, respectively.

In the National Health and Medical Research Council Report,[7] the adequacy of lactation at the time of discharge from the hospital was given for mothers in the two main diet groups in the Sydney Series. In this Series in the diet groups considered, there were 195 births; among these there were 3 stillbirths. Lactation data were given on 189 women only; no explanation could be found as to how the remaining 3 infants were fed. All of the 189 women breast fed their infants, 94 per cent of them fully, at the time of discharge from the hospital. At three months, lactation information on 193 women from both the Sydney and Melbourne Series was available. All of the 193 women were nursing their infants and 54 per cent of the women were fully breast feeding. From the lactation information in the Sydney Series one can infer a very high incidence of early breast feeding. The lactation data at three months from the two series, however, give no knowledge of the incidence at that time, only of the "adequacy" of lactation.

There are not many reports in the literature on the incidence and duration of breast feeding. The causes of failure are not always known and are seldom given. A report of the Ministry of Health of Great Britain in 1944[22] estimated that 80 per cent of the babies left hospitals in England wholly breast fed and that 95 per cent of the babies born in the district were breast fed when the midwife left the home, that at the end of 3 months 50 per cent of these babies, and at the end of 6 months 40 per cent, were still being nursed. The Plunkett Society[23] in New Zealand in 1943, on the basis of data obtained on 78 per cent of all infants of European stock, estimated the incidence of breast feeding in New Zealand as 89 per cent at 2 weeks, 71 per cent at 3 months, and 46 per cent at 6 months of age. Romero[25] states that in Mexico 92 per cent of the city children and 98 per cent of the country children are breast fed. Bain[24] reports on the incidence of breast feeding in 65 per cent of all births occurring in eligible

*The standard for complete breast feeding was that no supplementary milk formula was given, the supply of breast milk being sufficient for the baby's need for milk. Foods other than milk could be introduced at appropriate times.

hospitals in the United States during 1945. It was found for the group as a whole that 38 per cent of the infants were on the breast only at the time of discharge from the hospital, and that a smaller percentage of breast feeding occurred in hospitals in or near metropolitan areas as contrasted with areas removed from metropolitan centers. Most striking in these results were the regional differences, in the northeast the percentage of infants on the breast only at the time of discharge from the hospital was 23 as contrasted with an incidence of 55 per cent in the southeast. This wide range of incidence is also seen in the same environs: Byington[26] reports that breast feeding varies from 5.6 to 69 per cent in hospitals in the Detroit area. Rydberg[28] reports 33 per cent incidence of full breast feeding at 6 months and 7 per cent at 9 months in a group of 3,721 infants in Stockholm. Sundal[29] in a study of infants of 109 Oslo mothers found breast feeding entirely until 6 months in 36 per cent and until 9 months in 29 per cent. Toverud[30] reported the ability to lactate in a group of Oslo mothers given prenatal and postnatal care (including advice on meeting optimally the nutritional demands of pregnancy and receiving supplementary cod liver oil and brewer's yeast during pregnancy) to range from 49 to 63 and 49 to 62 per cent at 6 and 9 months, respectively.

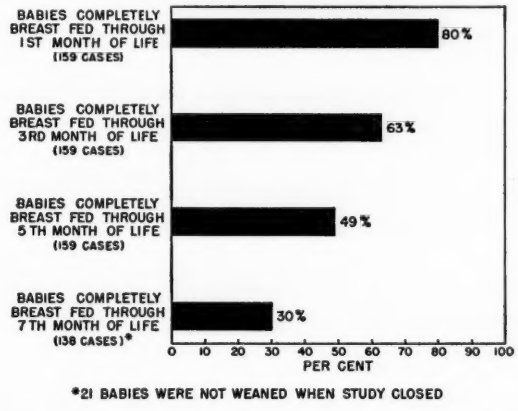
BABIES COMPLETELY BREAST FED THROUGH 1ST MONTH OF LIFE (159 CASES)
80%
BABIES COMPLETELY BREAST FED THROUGH 3RD MONTH OF LIFE (159 CASES)
63%
BABIES COMPLETELY BREAST FED THROUGH 5TH MONTH OF LIFE (159 CASES)
49%
BABIES COMPLETELY BREAST FED THROUGH 7TH MONTH OF LIFE (138 CASES)*
30%
0 10 20 30 40 50 60 70 80 90 100
PER CENT
*21 BABIES WERE NOT WEANED WHEN STUDY CLOSED

Fig. 2.—Percentage of babies completely breast fed in a study of 159 cases.

The question arises as to the cause of so great a variation in the number of women who feed their babies by the breast. In Mexico the expense of commercial milk that the poor classes cannot afford accounts for a very high incidence of breast feeding.[25] In the United States refusal and unwillingness on the part of the mother are probably most important in accounting for the high percentage of mothers not nursing their babies.[31, 32] Not only does the mother's attitude influence the course of lactation, but also the attitude of doctors and nurses who supervise breast feeding.

The attitude toward the clinical importance of breast feeding varies from country to country and from region to region. Thus an American author notes without critical comment that 23 per cent of the infants born in hospitals in the northeastern part of the United States are entirely breast fed, whereas a European author shows considerable concern about a hospital in which only 50 per cent of the babies are breast fed.[33] The results of artificial feeding vary with the place and country. Stevenson[34] compared experience of artificial feeding in Egypt with a comparative study in Chicago and with the Harvard Study. He stated, "For this [the Egyptian] group of people, in its present environment and culture, and notwithstanding the lack of supporting laboratory data,

we must conclude that breast feeding offers the only safe means of infant nutrition.'' From results of the Chicago Study Stevenson concluded that ''the practice of breast feeding is more successful, on a large population basis, than the practice of artificial feeding.'' For the Harvard Group, on the other hand, it was found that ''artificial feeding, when carried out properly from all standpoints by a selected group of mothers who are carefully supervised, compares favorably with breast feeding.''

Apart from these sociological, psychological, and physical factors that largely influence the incidence of breast feeding, there are various physiological factors, important among which is the diet of the mother during pregnancy and lactation that may influence her ability to breast feed.

Incidence in Relation to Maternal Diet.—The incidence of breast feeding related to maternal diet of the latter half of pregnancy is presented graphically in Fig. 3. It can be seen from the bar diagrams that only 6 per cent (2 cases out of 32) of the women in the ''very poor'' diet group completely breast fed their infants through the seventh month of life in contrast to 74 per cent (14 out of 19) in the "good or excellent" group. A consistent trend is shown for women on good diets to feed their babies longer, compared to women on poor diets. This trend was also evident in relation to diet ratings previous to pregnancy and during the first half of pregnancy.

The relatively large number of babies who ceased to be entirely breast fed by the seventh month, and their distribution among the four diet groups, indicates the existence of nondietary factors also associated with cessation of lactation. These nondietary factors were not investigated in the present study. However, Baby Health Centers, attended by many of the mothers in the study group, advised mothers to commence weaning of babies at about 6 months of age, and this probably accounts to some extent for the drop in breast feeding about this time.

The National Health and Medical Research Council[7] in investigating the ''adequacy'' of lactation among women with ''good'' and ''inadequate'' diets showed that, of the women who were nursing their infants at the time of discharge from the Sydney hospital, 97 per cent in the ''good'' diet group and 90 per cent in the ''inadequate'' diet group were fully breast feeding their infants. At 3 months post partum, of the women who were breast feeding, 66 per cent of the ''good'' and only 39 per cent of the ''inadequate'' diet group were still fully breast feeding their infants (Sydney and Melbourne Series combined).

Ebbs and Kelley[27] made a comparison of the incidence of breast feeding in three groups of low-income class mothers classified according to prenatal diet into either those who had a ''poor diet'' or those with ''supplemented diet'' or those taught a ''good diet.'' At 1 month the incidence was 67, 89, and 72 per cent, at 3 months 49, 63, and 60 per cent, and at 5 months 30, 44, and 43 per cent, respectively.

Macy and collaborators[35, 36] stressed the necessity of an adequate prenatal diet for successful lactation. They found that protein retention during pregnancy greatly influenced the ability of the mother to lactate. They found also a definite individual physiological capacity of the mammary gland in relation to both the quantity of milk produced and the length of time that lactation persists under normal circumstances. The development of the mammary gland again is dependent upon the general health and nutritional state of the mother.[2,b]

The effect of wartime undernutrition on the duration of lactation has been reported. The following from Antonov's report[18] is of particular interest:

> In 1918, on the basis of many observations of the effect of hunger on lactation in women, we came to the following conclusions: (1) in spite of hunger the mammary gland secretes milk if there is sufficient physiologic stimulation,

> that is, the capacity for breast feeding remains; (2) the quantity of milk, however, decreases; and (3) the duration of the lactation period becomes shorter. These circumstances were observed also during the siege of Leningrad, 1941 to 1943, with the difference that the mother's incapacity to produce sufficient milk was greater. . . . The capacity for breast feeding remained even in severe degrees of hunger, but less milk was produced and the breast feeding period was considerably shorter.

In the Wuppertal Study,[3] it was found that the percentage of mothers with successful "early lactation" (280 Gm. or more per day) fell slowly from 67 in 1937 to 31 in 1945 (the time of the most acute food shortage) and then rose to 43 in 1948. In the same Study results concerning "later lactation" among 400 mothers who gave birth in the Landesfrauenklinik in the second half of 1946 showed that after the second month the ability to lactate declined rapidly and that at 6 months only 5 per cent were fully breast feeding their children.

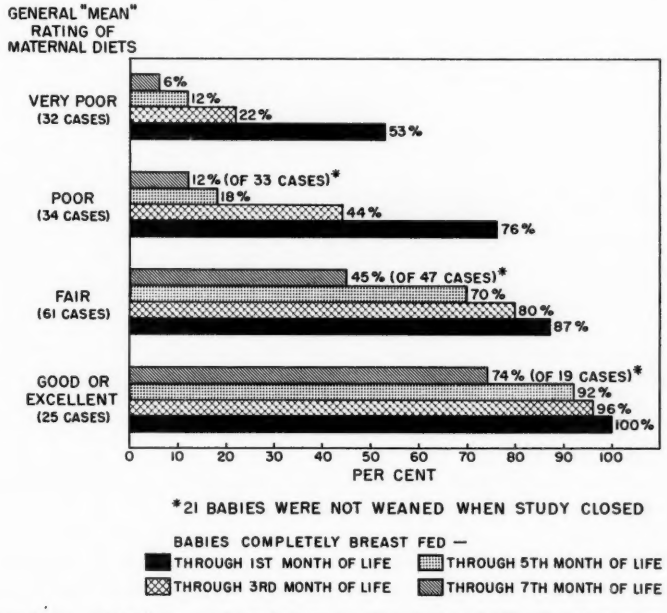

Fig. 3.—Breast feeding related to material diet in the latter half of pregnancy. Percentage of babies completely breast fed in each diet group.

The impressions of Dutch pediatricians and obstetricians regarding the effect of maternal undernutrition upon lactation were not in agreement with these findings. Most of them felt that, though slightly less milk had been secreted by the mother, the duration of breast feeding was not greatly affected.[19] Gunther and Stanier[4] state regarding the Dutch report: "It is possible that the women made greater efforts to suckle their children during the famine because there was little chance of feeding them in any other way." This desire to breast feed their children might have partially offset the harmful effect of starvation.

It appears from these findings that the level of prenatal nutrition in the mother is an important factor in determining whether or not she will be successful in breast feeding her infant.

Incidence Related to Pregravid Weight and Weight Gain During Pregnancy.—Table VIII shows the duration of lactation among the 31 subjects considered overweight when pregnancy began as compared with others in the

group. Table IX shows the number and percentage of babies in each of these two groups weaned by the end of the first month of life. A statistically significant relationship was found between prepregnancy obesity and early weaning, but no relationship was demonstrated between excessive weight gain during pregnancy and early weaning.

TABLE VIII. DURATION OF LACTATION IN SUBJECTS WITH PRECONCEPTIONAL OBESITY

	TOTAL NO. CASES	CASES WITHOUT LACTATION DATA	MONTH IN WHICH BABIES WERE WEANED											
			1	2	3	4	5	6	7	8	9	10	11	12
Obese patients	31	5	12*	0	1	2	2	3	0	3	1	2	0	0
Others	155	43	19*	15	12	12	6	10	2	12	13	9	0	2
Total	186	48	31	15	13	14	8	13	2	15	14	11	0	2

*Indicating a statistically significant relationship between preconceptional obesity and early loss of milk.

TABLE IX. DURATION OF LACTATION RELATED TO PRECONCEPTIONAL OBESITY

	TOTAL NO. CASES	BABIES WEANED BY THE END OF THE FIRST MONTH OF LIFE	
		NO. OF CASES	%
Obese patients	26	12*	46
Others	112	19*	17
Total	138		

*Indicating a statistically significant relationship between preconceptional obesity and early loss of milk. P=0.002.

Summary and Conclusions

The outcome of an inquiry into the incidence and duration of lactation in a group of Australian women has been presented. The duration was related to the level of maternal diet.

The incidence of lactation was shown to be high in contrast to that in many other areas in the world.

A consistent correlation between the duration of lactation and the level of maternal diet previous to and during pregnancy was found. Early weaning was shown to be associated with prepregnancy obesity, though not with excessive weight gain during pregnancy.

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THE USE OF VARIOUS ENDOCRINE PREPARATIONS IN THE SUPPRESSION OF LACTATION: A COMPARATIVE STUDY IN 800 CASES

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IN OUR modern civilization, the number of mothers who do not desire or are physically unable to nurse their babies has rapidly increased (50 to 75 per cent[1]) with the result that the artificial suppression of lactation has become a more or less necessary procedure. Abundant literature on this subject shows that many types of estrogens and androgens in various forms and combinations have been used and advocated by some, only to come into disfavor with others. Differing opinions also exist on the ideal time to start therapy in order to obtain optimum results.

Each product has certain merits and, unfortunately, often carries with it certain disadvantages. It was therefore decided to investigate a few of the various endocrines currently on the market with a view to evaluating and comparing the efficacy of each.

We consider that the ideal endocrine for suppression of lactation should meet the following requirements:

1. It should be rapidly absorbable.
2. It should be well tolerated with no side effects.
3. It should not cause withdrawal bleeding.
4. It should not require fluid restriction during therapy.
5. It should prevent breast engorgement and discomfort.
6. It should produce only a minimum amount of breast leakage.
7. It should not interfere with the onset of postpartum menstruation.
8. It should be administered orally.
9. The tablet or capsule should be not too large, and the number of doses should be few.
10. It should not be prohibitive in price to the average patient.
11. It should not predispose to breast complications.

As yet there has been no endocrine introduced to meet all these criteria. With further study and progress, however, we seem to be coming closer to our goal and from the findings of our study it appears that ethyl dimethyl allenolic acid* meets more of these criteria than most other drugs of a similar nature.

*Vallestril was supplied through the courtesy of G. D. Searle & Co.

Methods and Materials

Eight hundred cases were accumulated for this series from the Obstetrical Service of the Queens Hospital Center. All patients were observed while in the hospital for an average period of about five days, with particular reference to filling of breasts, pain, vaginal bleeding, and vaginal discharge.

Each patient was then given a follow-up questionnaire (Table I) to take home and instructed to return it, completed, to the hospital from three to four weeks post partum. This questionnaire included condition of the breasts, such as degree of fullness, degree of painfulness, and leaking, as well as an inquiry on vaginal discharge and vaginal bleeding.

TABLE I. QUESTIONNAIRE GIVEN TO 600 OBSTETRICAL PATIENTS FOR EVALUATION OF POSTPARTUM STATUS

1. Condition of breasts when you went home:
   (a) Very full ( ) (b) Very painful ( ) (c) Leaking much ( )
   Slightly full ( ) Slightly painful ( ) Leaking a little ( )
   Normal ( ) Normal ( ) Not leaking ( )
2. If your breasts bothered you, how long after you went home did it take for them to return to normal?
3. Did the vaginal discharge get heavier after you went home?
   ( ) Yes ( ) No
   Was it ever bright red in color?
   ( ) Yes ( ) No
   Have you had any bleeding like a regular period?
   ( ) Yes ( ) No
   If so, how soon after you went home? _____days, or _____weeks.

TABLE II. TIME OF RETURN OF BREASTS TO NORMAL AFTER INITIATION OF THERAPY

	OBSERVED IN HOSPITAL		FOLLOW-UP REPORT		
DOSAGE	NUMBER OF CASES	NO COMPLAINTS OR NORMAL WITHIN 4-5 DAYS (%)	NUMBER OF CASES	NORMAL IN LESS THAN ONE WEEK (%)	NORMAL IN MORE THAN ONE WEEK (%)
Vallestril.—					
3 mg. t.i.d. × 8-9 days	30	71	10	—	29
10 mg. b.i.d. × 1-2 days	86	60	30	30	10
10 mg. b.i.d. × 4-5 days	280	82	195	16	2
Stilbestrol.—					
3 mg. t.i.d. × 8-9 days	30	43	9	17	33
10 mg. b.i.d. × 1-2 days	79	60	35	—	59
10 mg. b.i.d. × 4-5 days	160	67	85	33	67
Tace.—					
1 capsule q.i.d. × 4-5 days	56	70	20	19	11
Placebo.—					
1 capsule b.i.d. × 4-5 days	50	42	23	26	32
Testosterone Cyclopentylpropionate.—					
200 mg. during labor	12	64	3	24	12
100 mg. during labor	9	40	3	40	20
100 mg. during labor and 100 mg. one day post partum	8	88	2	11	7

Our series, in which 415 patients responded to the questionnaire and 385 failed to reply, was divided into five groups, each group receiving a different endocrine. The medications used were ethyl dimethyl allenolic acid, chlorotriani-

sene,* diethylstilbestrol, and testosterone cyclopentylpropionate.† One group received only placebos. The drugs were employed in varying dosages. The exact dose of each drug, the number of days the medication was given, the daily frequency of administration, and the results are listed in Tables II to V. A group of patients was also given medication during labor and observed.

Table II summarizes the effects of the various endocrines used in this study with reference to the time of return of the breasts to normal; Table III, the effects on vaginal bleeding; Table IV, the effects on the amount and character of vaginal discharge, and Table V, the over-all postpartum results, classified as good, fair, and poor.

TABLE III. DEGREE OF VAGINAL BLEEDING FOLLOWING START OF THERAPY

	OBSERVED IN HOSPITAL				FOLLOW-UP REPORT		
DOSAGE	NO. OF CASES	NO. BLEEDING (%)	BLEEDING (%)	WITHIN 5 DAYS POST PARTUM (%)	NO. OF CASES	WITHIN 10 DAYS POST PARTUM (%)	MORE THAN 10 DAYS POST PARTUM (%)
Vallestril.—							
3 mg. t.i.d. × 8-9 days	30	81	19	40	10	20	40
10 mg. b.i.d. × 1-2 days	86	74	26	42	30	47	11
10 mg. b.i.d. × 4-5 days	280	86	14	50	195	38	12
Stilbestrol.—							
3 mg. t.i.d. × 8-9 days	30	60	40	50	9	17	33
10 mg. b.i.d. × 1-2 days	79	52	48	41	35	—	59
10 mg. b.i.d. × 4-5 days	160	60	40	—	85	33	67
Tace.—							
1 capsule q.i.d. × 4-5 days	56	78	22	50	20	—	50
Placebo.—							
1 capsule b.i.d. × 4-5 days	50	68	32	17	23	17	66
Testosterone Cyclopentylpropionate.—							
200 mg. during labor	12	82	18	40	3	—	60
100 mg. during labor	9	75	25	62	3	—	38
100 mg. during labor and 100 mg. one day post partum	8	94	6	65	2	30	5

TABLE IV. COMPARATIVE EFFECT OF VAGINAL DISCHARGE WITHIN 4 TO 5 DAYS AFTER INITIATION OF THERAPY

		HEAVIER DISCHARGE		WITH BRIGHT RED BLEEDING	
DOSAGE	NUMBER OF CASES	YES (%)	NO (%)	YES (%)	NO (%)
Vallestril.—					
3 mg. t.i.d. × 8-9 days	30	40	60	75	25
10 mg. b.i.d. × 1-2 days	86	50	50	40	60
10 mg. b.i.d. × 4-5 days	280	24	76	30	70
Stilbestrol.—					
3 mg. t.i.d. × 8-9 days	30	62	38	86	14
10 mg. b.i.d. × 1-2 days	79	54	46	67	33
10 mg. b.i.d. × 4-5 days	160	60	60	70	30
Tace.—					
1 capsule q.i.d. × 4 days	56	30	70	55	45
Placebo.—					
1 capsule b.i.d. × 4 days	50	58	42	68	32

*Tace was supplied through the courtesy of William S. Merrill Co.

†Depo-testosterone was supplied through the courtesy of The Upjohn Co.

TABLE V. COMPARATIVE RESULTS IN INHIBITION OF LACTATION WITH THE USE OF VARIOUS ENDOCRINE PREPARATIONS, AS DETERMINED ON DISCHARGE OF PATIENTS

DOSAGE	NUMBER OF CASES	RESULTS		
		GOOD (%)	FAIR (%)	POOR (%)
Vallestril.—				
3 mg. t.i.d. × 8-9 days	30	17	70	13
10 mg. b.i.d. × 1-2 days	86	50	30	20
10 mg. b.i.d. × 4-5 days	280	83	12	5
Stilbestrol.—				
3 mg. t.i.d. × 8-9 days	30	48	48	4
10 mg. b.i.d. × 1-2 days	79	58	38	4
10 mg. b.i.d. × 4-5 days	160	68	22	10
Tace.—				
1 capsule q.i.d. × 4 days	56	60	33	7
Placebo.—				
1 capsule b.i.d. × 4 days	50	21	53	26
Testosterone Cyclopentylpropionate.—				
200 mg. during labor	12	60	30	10
100 mg. during labor	9	43	14	43
100 mg. during labor and 100 mg. 1 day post partum	8	94	6	—

Summary of Literature

Only a brief review of some of the pertinent literature is presented. In 1947, an evaluation of estrogen therapy was made by Kimbrough and Israel[2] in which these authors reported that one of the most effective uses of natural or synthetic estrogens was their ability to prevent breast engorgement in the postpartum inhibition of lactation. They found that if therapy was started immediately after delivery, there was usually freedom from breast pain and engorgement and a distinct depression of lactation. When started after the onset of lactation, however, relief of the engorgement and subsidence of lactation were improved but not to any marked degree.

In contrast to this report, in the same year Coulton,[3] using Meprane, found no appreciable difference in patients receiving treatment before or after the start of lactation. His statistics on 183 cases showed that, among those patients who received treatment prior to the onset of lactation, results were excellent (complete inhibition with no toxicity) in 94.3 per cent of the cases. Therapy after the onset of lactation produced excellent results in 95.2 per cent. Even in the remaining cases where results were rated as satisfactory or fair, the breasts dried up two to three days after the patients' discharge from the hospital.

Since the initial popularity of stilbestrol and the conflicting reports on its value, many new agents have been introduced. Lubin,[4] in 1946, published his findings in 100 patients, dividing them into groups of 50 each, one receiving stilbestrol (diethylstilbestrol) 24 hours after delivery and the second group, no endocrine treatment whatsoever. In the former, he found lactation to some degree in 90 per cent and in the latter group, 100 per cent lactation. His conclusion was that in many instances stilbestrol only postponed engorgement and inhibited lactation to a slight degree, and he, therefore, questioned the advisability of giving it routinely to prevent painful engorged breasts.

In 600 cases treated with another product, ethinyl estradiol, Stewart,[5] in 1950, claimed better results than by any other method. Showing statistics on 150 of these patients, he reported that 84 per cent left the hospital with soft breasts and the remaining 16 per cent with varying degrees of firmness. In

this latter group, however, nursing had been attempted first and therapy started only from the third to the sixth postpartum day. Stewart also described elimination or reduction of withdrawal bleeding with this drug.

Reich and associates[6] placed 25 of their patients on Sulestrex* 24 hours after delivery and an additional 25 patients were not given the medication until lactation had started. Nine out of 10 patients were relieved of engorgement with treatment 24 hours after delivery. This percentage fell rapidly the longer they waited to start treatment. Once the mammae filled, less than half could be given relief with the medication alone. Adverse effects noted at follow-up examinations at six weeks included "rebound" engorgement in one patient requiring analgesics for relief of pain and dehydration, and minimal bleeding in one patient 16 days post partum, 6 days after lochia disappeared.

With the use of varying dosages of Dienestrol in 85 nonnursing mothers, Kosar and co-workers[7] found that only 13 per cent of the patients had complete inhibition. In contrast, in a control group of 75 patients who received no estrogens lactation was completely inhibited in 49 patients (65 per cent) by symptomatic therapy alone. Suppression of breast engorgement and pain were about the same in treated and untreated patients.

A very satisfactory report on a new estrogen (Tace) was published in 1953 by Nulsen and his co-workers.[1] In 100 cases, 97 had symptom-free suppression. Three patients (3 per cent) had painful filling after the cessation of the initial course and required a second course, whereas, according to earlier reports on the use of stilbestrol, 77.3 per cent required a second course. On Tace, very scant postpartum bleeding appeared in one of 100 cases (1 per cent) while 6 per cent of 1,711 patients on stilbestrol had such bleeding. The time when Tace was started did not seem to affect the results. It is believed that the elimination of withdrawal bleeding and recurrence of symptoms apparently occurred because this product was stored in the body fat and released gradually after the treatment was stopped.

A number of investigators have been using androgen-estrogen combinations for the suppression of lactation. Kurzrok and O'Connell[8] were the first to employ androgens for this purpose. Katzman[9] reported that painless lactation resulted in 88 per cent of patients from a 1 c.c. intramuscular dose of androgen-estrogen combination (Gynetone,† during the first 24 hours post partum and inhibition of lactation in 97 per cent of patients from a single intramuscular dose of 2 c.c.

In additional studies in 1954 by Dodek, Friedman, Soyster, and Marcellus,[10] a single intramuscular injection of 100 mg. of testosterone cyclopentylproprionate in cotton seed oil (Depo-testosterone) in 125 patients during the intrapartum or early postpartum period was sufficient to suppress lactation. Of these, 25 patients received the injection within five hours post partum. Good results were obtained in 90.4 per cent but these authors stated that in practically all patients except for 5 cases, swelling of the breasts occurred.

Comment

Suppression of lactation has become not only an accepted medical procedure, but one that is demanded by the public. As a result of this, the physician has been confronted with innumerable reports on the efficacy of many endocrine products on the market. In general, each investigator has obtained more or less good results with whatever product he used.

*Abbott Laboratories.
†Schering Corporation.

From the reports of other investigators, and from our own experience, good results are obtained with almost any of the endocrines as long as the hormone is started sufficiently early post partum and continued long enough so as to inhibit the anterior pituitary production of prolactin. We believe this has been substantiated in the report of Kimbrough and Israel.[2]

We wish to summarize some of the theories published, in addition to our own, in an attempt to explain the possible modus operandi of suppression of lactation. Living tissue and organs function by necessity. During normal physiological function these organs react to demands of their dependent tissue. As soon as an organ begins to function independently a pathological condition results. The anterior pituitary gland, being the master endocrine control, also responds to demands of its dependent hormone-producing tissues. It appears to operate by a rheostat mechanism and its secretion of the particular hormones is controlled by the concentration of the resulting endocrines present in the circulation.

For example, follicular stimulating hormone (FSH), luteinizing hormone (LH), and luteotropin are secreted by the anterior pituitary until the concentrations of estrogen and progesterone have reached their peak in the vascular tree and are then inhibited. After a period of several days, desquamation of the endometrium takes place. When pregnancy supervenes, the corpus luteum has to continue and since the FSH and LH are no longer secreted by the pituitary, an auxiliary organ, the placenta, takes over the function of producing the pituitary-like hormone (chorionic gonadotropin), thus serving to prolong the life of the corpus luteum. The function of the latter is necessary until there are sufficient chorionic villi to take over and produce the high level of estrogen and progesterone so vital for the continuation of the pregnancy.

From this concept it would logically follow that the anterior pituitary may not secrete any gonadotropin during the entire pregnancy. (The concentration of estrogen and progesterone is far above the peak necessary to inhibit the secretion of the pituitary gonadotropin.) When the high estrogen and progesterone concentration is lost by the expulsion of the placenta, the anterior pituitary is no longer inhibited and its gonadotropins are again secreted. The luteotropin or prolactin at this time seems to effect a strong secretary influence on the mammary glandular system, which has also had a prolonged proliferation and priming throughout pregnancy by estrogens and progesterone. It is also accepted by many that the humoral or suckling reflex contributes toward the continuation of the prolactin secretion already initiated.

It would seem that the breasts must have their glandular system prepared and primed by estrogen and progesterone for a long period of time before they will respond to the prolactin stimulant. This possibly explains why the glandular system of the breast is not stimulated to secretion in the nonpregnant woman. It appears to be similar to the functioning of the endometrium which first has to be primed by estrogen before its secretory activity is affected by progesterone.

An attempt should also be made to explain why a number of nonnursing mothers do not require endocrines for suppression of lactation. This may occur because in a certain percentage of patients the follicular apparatus of the ovary may become activated very soon post partum and thus supply the necessary amount of estrogen to inhibit the anterior pituitary and in turn prevent the release of the prolactin.

Masson[11] showed that he was able to suppress lactation in mice with the use of pregnant mare serum. This suppression, he was able to demonstrate, was due to secretion of estrogen and progesterone by the ovary. Sharman[12] showed that 33 per cent of lactating mothers have a return of menstruation within 12 weeks post partum compared to 91 per cent of nonlactating patients. If 33 per cent of the nursing mothers resume their periods within 12 weeks, that means the follicular apparatus becomes activated soon post partum. This would indicate that there is some break-through in the secretion of FSH of the anterior pituitary in some of the lactating patients. It would also clarify the fact that a certain percentage of mothers who attempt to nurse fail to have sufficient secretion of milk.

The minimum dose of specific endocrine required to suppress lactation appears to depend on its ability to keep the anterior pituitary inhibited against release of prolactin for the necessary number of days post partum. One may perhaps hypothesize that the length of time necessary for the administration of any endocrine is, to some degree, dependent on how early the follicular apparatus of the ovary resumes its activity. At this time there is sufficient estrogen from the follicles to keep the pituitary inhibited from further release of the prolactin.

The only differences that seem to result from any one product as compared with another are, first, in regard to vaginal bleeding (withdrawal bleeding) and, second, the objections that some patients express to one or another product because of the form of administration (parenteral use, size of capsule, frequency of dosage).

According to our findings, ethyl dimethyl allenolic acid, 20 mg. daily for four to five days, beginning immediately post partum, has given results as good as, if not better than, any product heretofore reported upon.

Our general observations on the effects of Vallestril, in addition to observations in a considerable number of private cases (not included in this series), warrant our feeling that this drug does have sufficient merits to be recommended for use in the suppression of lactation. Further studies and a greater number of statistics may ultimately bear this out more strikingly. It is necessary to bear in mind that the type of clinic patient who answered our subjective questions was not always reliable and her responses not completely accurate. Judging from all cases observed until discharge from the hospital, however, it was our impression that Vallestril had given very good results in regard to prevention of engorgement of breasts, vaginal bleeding, and lack of discomfort.

We regret that we were unable to duplicate the results reported in the literature on the effects of testosterone cyclopentylpropionate administered during labor. In 8 cases, by giving a total of 200 mg. in two equally divided doses, one during labor and one 24 hours post partum, we succeeded in confirming the earlier reports (Table V). The question still remains debatable, however, of the advisability of using such large doses of androgens during the reproductive age.

Summary

1. In view of the increasing popularity of artificial suppression of lactation, we have presented a comparative study of 800 cases, illustrating the effects of various endocrines on the market.

2. Eleven criteria for the ideal endocrine for inhibition of lactation are listed.

3. Eight hundred cases were followed during the five days post partum and some by questionnaires given to patients and returned to the hospital three to four weeks post partum.

4. Four tables show the effects of the various products on the suppression of lactation, breast engorgement, vaginal (withdrawal) bleeding, and vaginal discharge.

5. A brief review of the pertinent literature is presented.

6. Some explanation of the possible modus operandi of the suppression of lactation is offered.

7. We conclude that ethyl dimethyl allenolic acid (Vallestril), 20 mg. daily for four to five days post partum, is effective in the suppression of lactation.

8. We feel that these preliminary results warrant further studies to confirm our present findings.

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MAN'S ASSUMPTION OF THE ERECT POSTURE— ITS EFFECT ON THE POSITION OF THE PELVIS*

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IN AGES past, the ancestor of man was perhaps a stocky quadruped who, because of a changing environment and the need for greater protection against his enemies, endeavored to raise the torso and increase the visual horizon. The gorilla accomplished this objective through the elongation of the upper extremities by which means the head could be raised and supported for observation. Man is supposed to have assumed the erect posture by rotating the pelvis upon the femora until the abdominal and pelvic cavities were vertical, balance being maintained through the development of strong back muscles and curves of the vertebral column in the lumbar and dorsal regions.

The direction of visceral support was changed with the new position and, as obstetrics, gynecology, and orthopedics developed, interpretations dependent upon pelvic rotation were applied. In the practice of obstetrics the mechanism of labor, after engagement, was not altered with the changed position; but unengagement of the fetal head may be due to faulty interpretation of the relationship between the long axes of the abdominal and pelvic cavities.

The gynecologist is concerned with the relation of the bony pelvis to the long axis of the abdominal cavity, especially when confronted with the problem of prolapse of the pelvic viscera. For example, those who believe that the abdominal and pelvic cavities are in the same vertical plane are inclined to suspend a prolapsed vaginal vault to the anterior abdominal wall. Repeated failures and an occasional enterocele thereafter suggest that intra-abdominal pressure on the viscus and its supports was increased by transplanting a pelvic organ into the abdominal cavity.

The orthopedist who accepts the theory of pelvic rotation may be at a loss to explain the relative freedom from pain in the symphysis and in the sacroiliac joints as weight is transferred along an angulated pathway extending from the sacrum to the femora. These and other problems will eventually be solved; until then let us scrutinize the pelvis and perhaps certain obvious findings may be called to our attention which when applied may increase the field of therapy.

The acetabulum, ischial tuberosity, pubis, and sacrum may be specific anatomical terms, but collectively they are parts of a structure termed the pelvis in which are suspended the various viscera and through which the fetus must pass to be delivered. A three-dimensional impression of the pelvis

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in which the roof, floor, sides, inlet, and outlet are as accurately placed as are the ceiling, walls, and floor of a room is a prerequisite for further enlightenment. After the establishment of a standard position of the pelvis during the act of lifting, it will be possible to determine the position of the various components of the pelvis when the patient lies on the table for delivery or gynecological surgery, by rotating the entire pelvis through an arc of 90 degrees.

With the advent of roentgen pelvimetry a new method for the study of pelvic architecture became available. An anteroposterior view of the pelvis revealed a view as represented in Fig. 1. Contrary to one's expectations it does not show the external surface of the body of the pubic bone but instead a view into the cavity of the pelvis. This finding suggests that the pelvic and abdominal bores are not vertical but that they are angulated at the superior

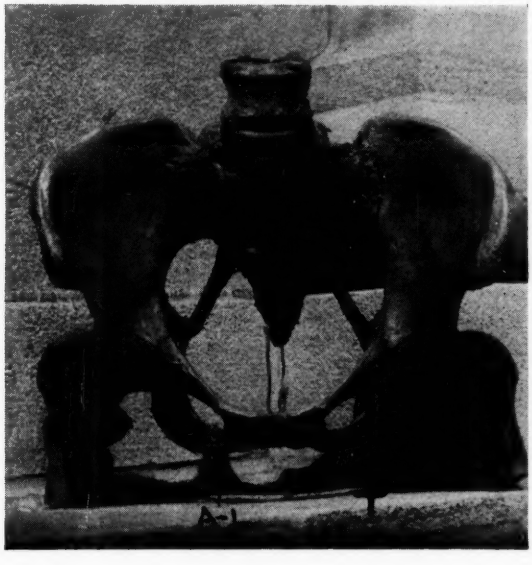

Fig. 1.—A drawing from an anteroposterior roentgenogram of the pelvis is a view into the bore of the pelvis; very little of the body of the pubic bone is seen. It suggests that the pelvic cavity is horizontal.

strait. A lateral roentgenogram confirms this impression but an inclination far greater than the angle of 35 to 45 degrees, the average angle suggested by a group of polled obstetricians, is revealed. Readings ranging from a 60 to 80 degree inclination are not infrequent. Many variables enter a roentgen study which preclude its use to determine the standard angle at which the abdominal and pelvic cavities meet at the superior strait.

During the act of heavy lifting or carrying, the torso is held erect so that weight is transmitted in a vertical direction through the pelvic bone to the femora. A correlation between atrophied and hypertrophied pelvic structures may aid us in determining the exact position of its component parts: for it is generally agreed that structures of the body not often used tend to atrophy, while structures which are under stress and strain will hypertrophy. The

tuberosity of the ischium, Fig. 2, is a splendid example of hypertrophy and represents the result of traction by the hamstring muscles which are attached to this area and course to the region of the knee. Disuse is suggested by the notch in the acetabulum and suggests that it supports very little of weight-bearing.

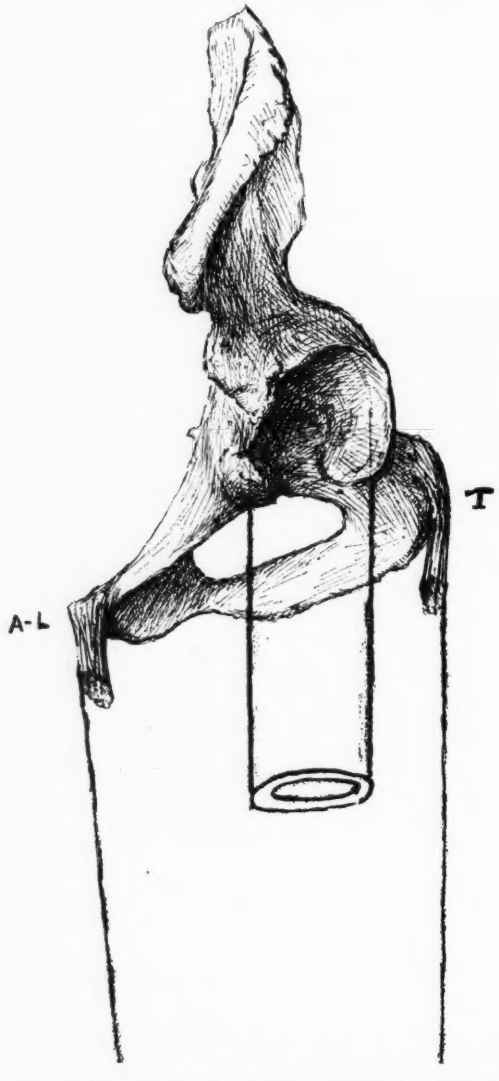

Fig. 2.—The upper end of the femur has been removed to expose the acetabulum. That portion subjected to most stress is hypertrophied, while the notch represents atrophy due to disuse. *A-L* represents the adductor longus muscle which flexes and adducts the thigh. *T* is the origin of a group of muscles which extend the thigh. To function as extensor muscles, the tuberosity of the ischium must be posterior to the shaft of the femur.

With these facts in mind, let us endeavor to draw conclusions from a close analysis of function in the pelvic bone. When the head of an erect femur is engaged in the acetabulum the tuberosity of the ischium must lie posterior to the shaft if it is to serve as the origin of a muscle which draws the knee backward. With this functional relationship the symphysis and the arch of the

pubis are practically horizontal. If the pelvis is rotated until the inlet inclines 35 degrees, the tuberosity of the ischium will no longer be posterior to the shaft but medial to it. With any inclination of the superior strait less than 80 degrees the muscles attached to the tuberosity of the ischium will no longer draw the thigh posteriorly but toward the midline; walking thereby is impossible. Thus we see that the pelvis is an integral part of the lower extremity and cannot be rotated to assume the erect posture without altering muscular action and function.

Fig. 3.—Showing the sacrum and right half of the pelvis. *A-S* is the heaviest segment of the brim and represents the pathway through which weight is carried to the head of the femur. *A-P* is the stabilizing arm.

To verify the foregoing statement, the hip joint will next be analyzed. Through this joint, weight is transferred from the torso to the limbs and therefore it may contain certain markings which may indicate in which position the pelvis should articulate with the femur in order to carry the greatest amount of weight efficiently. The femoral ball-and-socket joint consists of a globular head articulating in the cup-shaped acetabulum. With the exception of a rough depression on the medial surface of the head of the femur, which serves as the attachment of the ligamentum rotundum, the entire head is smooth and accepts weight transference whether flexed or extended. The femoral head, therefore, contains no markings which could be of value in verifying our assumption. The acetabulum, which maintains the same relative position whether standing or sitting erect, should next be analyzed. So let us

engage a disarticulated femoral head in the acetabulum so that the incisura or weakest segment carries least weight. With this efficient articulation the inlet of the pelvis is vertical. Rotation of the pelvis until the inlet inclines 35 degrees will place the incisura of the acetabulum near the segment of the globular head accepting most weight. Instability and a tendency toward dislocation increase as the inlet is rotated toward the horizontal but diminish as it is rotated to vertical.

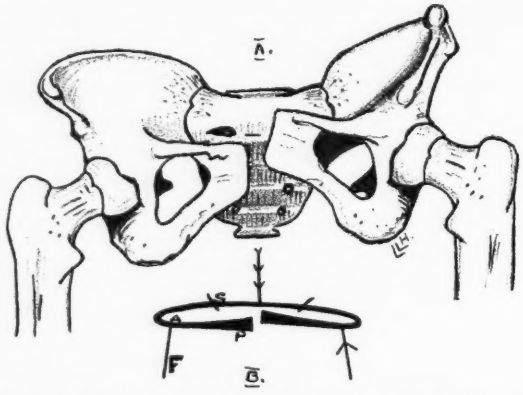

Fig. 4.—The pelvis is rotated on the femora until the inlet is horizontal. The abdominal and pelvic cavities are in the same vertical bore. The body of the pubic bone lies in the plane of the anterior abdominal wall and appears to be posterior to the mons veneris. With each step, weight is transferred from the sacrum through a horizontal lever *S-A* to the femur. Since there is no fusion of the symphysis there should be an alternating rise and fall of the *A-P* arm with concomitant instability and discomfort.

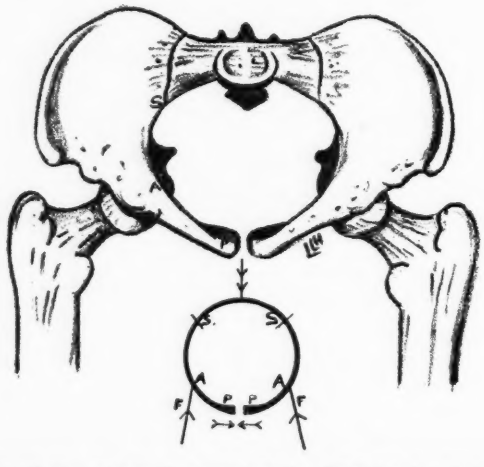

Fig. 5.—The cavity of the pelvis is horizontal. Weight is transferred from the sacrum through the vertical ridge *S-A* to the head of the femur. A stabilizing force traversing *A-P* forces both pubic bones together at the symphysis and thereby stabilizes the sacroiliac and symphysial articulations.

On the brim of the pelvis, Fig. 3, a distinct ridge of hypertrophied bone, *S-A*, will be seen to extend from the wing of the sacrum to the acetabulum (sacroacetabular ridge). It represents the pathway through which weight is transferred from the torso to the head of the femur. Between the acetabulum and the pubic bone the ridge is less definite and suggests that a stabilizing force traverses this segment (acetabulopubic ridge).

In Fig. 4, the pelvis has been rotated until the abdominal and pelvic cavities are in the same vertical bore. The inlet of the pelvis now rests upon the head of the femur like a lever, the sacroacetabular ridge and the acetabulopubic ridge being the two arms of a lever while the femur acts as the fulcrum. With each step, weight is transferred from the sacrum through the sacroacetabular arm to the head of the femur and at the same time there should be a concomitant rise of the acetabulopubic arm detected as a gliding in the symphysis. Such instability should elicit pain in the sacroiliac articulation; that this is not the case suggests that the brim is not rotated upon the femora.

The pelvis in Fig. 5 has been rotated until the sacroacetabular ridge is a vertical extension of the erect femora; sudden weight transference, as in jumping, will force the two halves of the pelvic brim together, thereby contributing toward stability without the necessity for fusion.

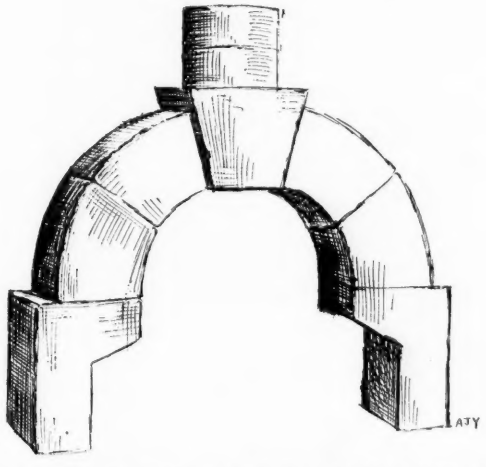

Fig. 6.—An arch is a structure by means of which weight is transferred around an opening to a column by means of an arched segment. The sacrum may be substituted for the keystone, the sacroacetabular ridge for the arc, and the femora for the columns. Greatest weight can be supported when the arch and the columns are in the same vertical plane.

Examination of an emaciated woman standing erect will verify many of the statements enumerated. The promontory of the sacrum often can be felt close to the anterior abdominal wall slightly distal to the umbilicus. The bodies of the pubic bones will lie horizontally between the femora. During the act of lifting, a line drawn from the promontory of the sacrum to the symphysis of the pubis is almost vertical. The tuberosity of the ischium is readily detected posterior to the shaft of the femur, the distance from the shaft being increased by leaning forward as in climbing a hill. These various confirming factors suggest that the pelvic cavity is encased within a bony structure which not only serves as the origin or insertion of muscles, but it also contains an arch through which weight is transferred around an opening to the heads of the femora.

A comparison of the arch used in building with the arch within the pelvis may further enlighten us on the probable position of the pelvis when erect.

Fig. 6 represents a typical arch. The central mass is a keystone which may be compared with the sacrum; the arched segment may be detected as the sacro-acetabular ridge and the columns as the femora. The greatest weight can be supported when the arch and the columns are in the same vertical plane.

This efficient principle is applied in building construction, but the Master Builder is not to be outdone by man, for in the human being the pelvic inlet or arch is in line with the femora or columns when heavy weight is being transferred from the torso to the femora.

Fig. 7.—The human torso of the Centaur is erect upon the forequarters, in man the torso is erect upon the hindquarters.

A composite picture of our findings is represented by Fig. 7. It conveys the impression that the abdominal and pelvic cavities are at right angles to each other. Man, therefore, is unique and distinctly differs from his ancestors, for his hindquarters, which include the pelvis and attached limbs, are like those of the quadruped; but the torso is acutely angulated at the lumbosacral junction. In many ways man resembles the mythical Centaur from the Isle of Thessaly whose sculptured form on the friezes of various Greek buildings may be a bardic reference to the time when quadruped man angulated the torso on the hind quarters for observation and protection.

Summary

It appears that man assumed the erect form by angulating the lumbosacral area at the sacrum. The pelvis was not altered with this change and

it therefore bears the same horizontal relationship to the limbs attached thereto as does the pelvis of a quadruped to its hind limbs. This concept of the relationship between the pelvic and abdominal cavities may suggest some alterations in our established gynecological and obstetrical procedures.

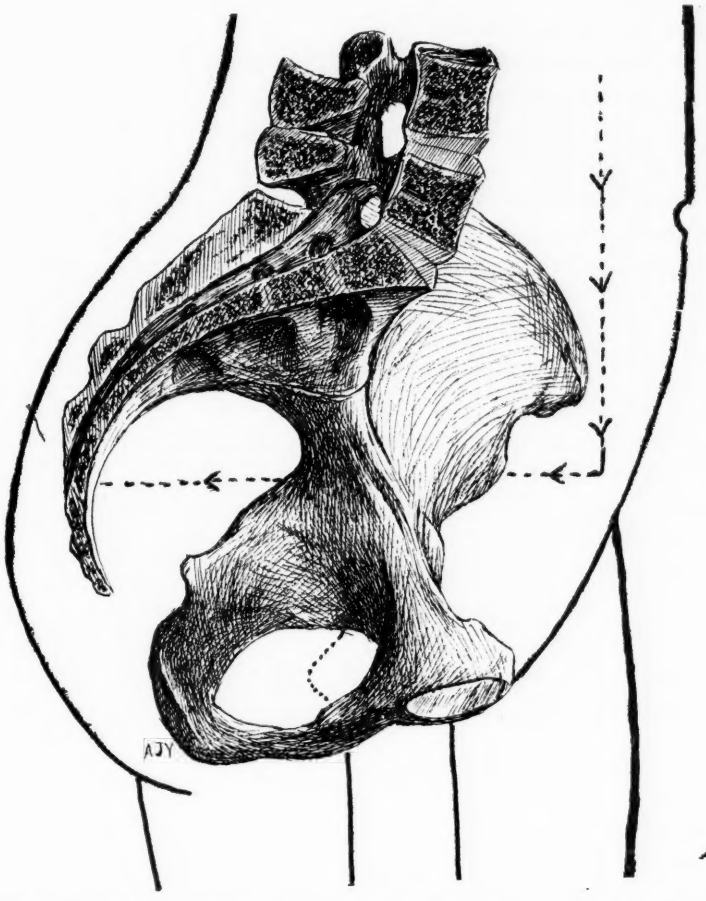

Fig. 8.—The left half of the pelvis rests upon the femur in such a position that the notch in the acetabulum carries least weight. The inlet of the pelvis is vertical and the bodies of the first and second sacral vertebrae and the bodies of the pubic bones are horizontal. The cavity of the pelvis is at right angles to the cavity of the abdomen.

Conclusions

1. The pelvis is an integral part of the lower extremity and it cannot be rotated from a horizontal bore to a vertical bore without disrupting muscular function.

2. The pelvis did not rotate when man stood erect.

3. Man assumed the erect posture through a series of changes, the most important of which was the angulation of the vertebral column at the sacrum.

4. The cavity of the pelvis is at right angles to the cavity of the long axis of the abdominal cavity.

5. In the lifting position the inlet of the pelvis is practically perpendicular.

6. When the individual stands erect or is seated on a saddle, the body of the pubic bone is horizontal.

7. In the sitting position the pelvis bears the same relationship to the abdomen as it does in the erect position.

8. The bodies of the first two sacral vertebrae are parallel to the body of the pubic bone, hence horizontal.

9. On the delivery table, the body of the pubic bone is perpendicular, and the inlet of the pelvis is parallel to the floor.

10. The soft, thin skin of the anterior abdominal wall resembles the underbelly of a quadruped which has rotated from a horizontal to a vertical position.

11. The mythical Centaur may be a bardic reference to the time when man could raise and lower the torso.

12. Moving the erect torso of a Centaur from the forequarters to the hindquarters constructs a form closely resembling that of man.

THE FLAT SACRUM: ITS IMPORTANCE IN OBSTETRICS

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MANY authors in the past would have us believe that the curved sacrum is the normal one and that variations are abnormal. Mayer and Morin[1] classify sacra into two categories: The curved or dynamic and the straight or static sacrum. Hensen,[2] in his study of one hundred cases with unengagement at the onset of labor, classified his sacra into four groups, the last, or type IV, being the straight sacrum. Roth[3] designated six types of sacra on the basis of the degree of curvature.

The inclination of the sacrum exerts an obvious influence on the antero-posterior diameters along the birth canal. Encroachment on the capacity of the posterior segment of the pelvis at the various levels is determined also by both degree of sacral curvature and angle of sacral inclination. The transverse diameters of the bony pelvis play an important role in the outcome of labor and are dependent upon such factors as splay of the walls and prominence of the ischial spines. Combined with the sacral configuration, all other pelvic characteristics go to form a fairly fixed and measurable factor in labor. Maternal powers and malleability of the fetal head are more variable factors.

Because it was our impression that many patients who were delivered by cesarean section had pelvimetric examinations which were reported as presenting a flat sacrum, we decided to study the material available at the Bronx Hospital.

Clinical Material and Method of Study

This study encompasses all deliveries performed at the Bronx Hospital and all pelvic x-ray studies made at this institution from Jan. 1, 1948, through Dec. 31, 1952. A total of 12,787 deliveries were performed during the period under study. Of these, 2,068 patients, or 16.3 per cent, underwent x-ray pelvimetry. Four hundred and forty, or 21.3 per cent of the latter, showed a flat sacrum (Table I). Roth[3] found 44, or 17.2 per cent, straight sacra in a study of 256 primiparas. Snow[4] reports a 25 per cent incidence of flat to convex sacra.

Table I. Total Deliveries, Frequency of X-ray Pelvimetry and Incidence of Flat Sacra According to Year

Year	Deliveries	Cases X-rayed	Percentage X-rayed	Total Flat Sacra	Percentage of Flat Sacra among X-rayed Cases
1948	2,609	320	12.3	66	20.6
1949	2,424	325	13.4	70	21.5
1950	2,611	424	16.3	102	24.1
1951	2,656	486	18.3	101	20.8
1952	2,437	513	21.1	101	19.7
Total	12,737	2,068	16.3	440	21.3

TABLE II. TYPES OF DELIVERY IN FLAT-SACRUM GROUPS AS COMPARED WITH ALL DELIVERIES (1948-1952)

	SPONTANEOUS				LOW FORCEPS				MIDFORCEPS				BREECH				CESAREAN					
YEAR	FLAT SA-CRUM	% FLAT SA-CRUM	ALL DEL.	% ALL DEL.	FLAT SA-CRUM	% FLAT SA-CRUM	ALL DEL.	% ALL DEL.	FLAT SA-CRUM	% FLAT SA-CRUM	ALL DEL.	% ALL DEL.	FLAT SA-CRUM	% FLAT SA-CRUM	ALL DEL.	% ALL DEL.	FLAT SA-CRUM	% FLAT SA-CRUM	ALL DEL.	% ALL DEL.	TOTAL FLAT SA-CRUM	TOTAL DELIV-ERIES
1948	28	42.4	1,934	74.1	13	19.7	424	15.8	8	12.1	92	3.4	3	4.5	73	2.8	14	21.2	85	3.3	66	2,609
1949	28	40.0	1,726	71.2	11	15.7	401	16.5	10	14.3	131	5.4	7	10.0	66	2.7	14	20.0	102	4.2	70	2,424
1950	42	41.6	1,874	71.3	22	21.6	418	16.0	7	6.9	110	4.1	13	12.7	76	2.9	20	19.6	141	5.4	102	2,611
1951	52	51.5	1,857	69.2	16	15.8	443	16.7	10	9.9	133	5.0	9	9.0	68	2.6	16	15.8	151	5.7	101	2,656
1952	39	38.6	1,642	67.4	25	24.8	463	19.0	14	13.9	155	6.3	10	9.9	61	2.5	14	13.9	153	6.4	101	2,437
Total	189	42.8	9,033	70.6	87	19.8	2,149	16.8	49	11.1	621	4.8	42	9.6	344	2.7	78	17.7	632	4.9	440	12,737

The Snow technique was used consistently and all x-rays were read by the resident of the Radiology Department, checked by the Attending Radiologist, and finally reviewed by the authors of this paper. Only those x-rays which showed a totally flat sacrum were chosen for study. Pelvimetric studies by x-ray were undertaken for the usual indications.

In each of the 440 flat sacra, the labor and outcome were analyzed. Measurements were closely reviewed with specific attention to abnormalities and types of pelvis. The characteristics of the delivery were recorded and comparison was made with the over-all records for deliveries at this institution over the same period of time.

Pelvic Contractions.—

According to the Snow[4] technique of x-ray pelvimetry, the normal ranges for the major diameters of the pelvis are:

True conjugate	10.5 cm. to 11.5 cm.
Transverse of the inlet	11.5 cm. to 12.5 cm.
Anteroposterior of the midpelvis	11.0 cm. to 12.0 cm.
Interspinous	10.0 cm. to 11.0 cm.
Posterior sagittal	7.0 cm. to 8.5 cm.
Intertuberosity	9.5 cm. to 10.5 cm.

Considering diameters with measurements below the lower normal value of Snow[4] to be contracted, 160, or 36.4 per cent, of the 440 patients with flat sacra were found to have one or more diameters contracted. The number of contracted diameters was as follows:

True conjugate	39
Transverse of the inlet	16
Anteroposterior of the midpelvis	28
Interspinous	94
Posterior sagittal	25
Intertuberosity	48

In several cases, there was a combination of contracted measurements rather than a solitary one. These were as follows:

True conjugate and anteroposterior of the midpelvis	14
True conjugate, anteroposterior of the midpelvis, and posterior sagittal	3
Transverse of the inlet and interspinous	7
Transverse of the inlet, interspinous, and intertuberosity	3
Interspinous and intertuberosity	29

Contractions of the interspinous and intertuberous diameters, either singly or in combination, appear to be a frequent finding among the 440 cases of flat sacra. The interspinous diameter was contracted in 21.4 per cent of the cases. The intertuberous diameter was contracted in 10.9 per cent of the cases and a combination of both of these contractions occurred in 6.6 per cent of the cases.

Types of Delivery.—

Table II compares deliveries performed on all patients from January, 1948, through December, 1952, at the Bronx Hospital with those performed on the selected group with flat sacra. Of the 12,737 births in the period under study, 9,033, or 70.6 per cent, terminated spontaneously as opposed to 189, or 42.8 per cent, spontaneous deliveries in the flat sacrum group. In 621, or 4.8 per cent, of the unselected group, midforceps were resorted to, whereas midforceps were used in the flat-sacrum group in 49 cases, or 11.1 per cent. It was observed that 344, or 2.7 per cent, of all deliveries were breech presentations and 42, or 9.6 per cent, of the flat-sacrum group were breeches. Cesarean sections were

performed on 632, or 4.9 per cent of all patients delivered at this institution, whereas 78, or 17.7 per cent, of the selected group were delivered abdominally.

A comparison of the indications for cesarean section in the patients of the flat-sacrum group with the over-all indications at this institution, as reported in a previous paper,[5] is of interest (Table III). Although 22.3 per cent of all sections were performed for cephalopelvic disproportion, this figure rose to 62.8 per cent in the flat-sacrum group. There were 27.3 per cent sections performed for previous sections in the unselected group. In the flat-sacrum group, there were only 2 repeat sections, or 2.6 per cent, in both of which the indication for the original operation had been cephalopelvic disproportion. The incidence of cesarean section for abnormal presentation in the straight-sacrum group is almost double that in the over-all nonselected group, being 15.3 per cent and 8.7 per cent, respectively. No patient in the group with straight sacra was subjected to cesarean section for ante- or intrapartum hemorrhage.

TABLE III COMPARISON OF INDICATIONS FOR CESAREAN SECTION

INDICATIONS	PERCENTAGE IN FLAT-SACRUM GROUP	PERCENTAGE IN ALL DELIVERIES
Cephalopelvic disproportion	62.8	22.3
Previous section	2.6	27.3
Abnormal presentation	15.3	8.7
Toxemia	8.9	4.2
Fetal distress	2.6	5.9
Hemorrhage	0.0	14.9
Others	7.8	16.7

The incidence of operative delivery was approximately doubled in the flat-sacrum group. Midforceps were resorted to 2.3 times as often in this group, while cesarean sections were performed 3.6 times as frequently.

Midpelvic Arrest and Cephalic Transverse Position.—

Steele and Javert[6] state, "The lateral flexion of the head forward preceding internal rotation is effected by the shunting action produced when the rounded vertex strikes the lower curve of the sacrum and fails to occur when the sacrum is long and straight and the lateral bore of the pelvis is divergent. It is often under such circumstances that the head becomes arrested in the posterior pelvis, the Transverse Arrest."

As previously stated, midforceps were resorted to in the flat-sacrum group 2.3 times more frequently than in the over-all group. Transverse position of the vertex during engagement occurs usually in two types of pelves: (1) where the pelvis is large and the vertex small, and (2) where the pelvis is flat and the anteroposterior diameters are shortened. Rotation of the vertex at the midpelvis may be impossible in the presence of a flat sacrum. Delivery from below in these cases can be accomplished only if the vertex bulges the pelvic floor, thus allowing for rotation at the outlet. In attempting vaginal delivery with a transverse position of the vertex arrested in the midpelvis, the obstetrician must know the condition of the sacral curve. With a flat sacrum, forceps rotation should not be attempted at the midpelvic level. Instead, traction to the pelvic floor with rotation at the outlet should be the mode of delivery.

Snow[4] contends that the majority of flat sacra sweep backward. A vertex held up in the midpelvis may suddenly pass through and deliver precipitately, ripping the perineum. We have all seen, much to our chagrin, in the case scheduled for cesarean section because of midpelvic arrest with no progress, the vertex suddenly pass through the midpelvic contraction and proceed to a rapid spontaneous delivery. This is more likely to happen when the sacrum is flat, with a posterior sweep, thus increasing the posterior sagittal diameter.

Effects on Labor.—

The average length of labor is eighteen hours in primiparas and twelve hours or less in multiparas, according to DeLee.[7] Using this as a criterion, we found 171, or 38.6 per cent, of our flat-sacrum cases to have prolonged labor. Correcting this figure by eliminating 15 cases that were sectioned electively, 40.2 per cent had prolonged labor. It is not difficult to correlate this finding with what we have already said. Midpelvic contraction, absence of sacral curve, and presence of transverse vertex position all tend to increase the length of time a patient must labor to overcome these obstacles.

Conclusions

The flat sacrum presents several problems to the obstetrician. It may be associated with various types of pelvic contractions. The anterior-posterior pelvic diameters may be contracted when the flat sacrum inclines forward. The transverse pelvic diameters are often found shortened, as the funnel-type pelvis is frequently found associated with the flat sacrum. The incidence of prolonged labor and that of operative delivery are often increased. The obstetrician should be forewarned that despite a prolonged labor, if the flat sacrum inclines backward, the second stage of labor may terminate precipitously with a deep perineal laceration. Attempts at midforceps delivery in the presence of a flat sacrum may often be impossible if rotation is attempted in the midpelvis. Traction should first be applied to the vertex in the transverse position until the presenting part bulges the perineum. Rotation may then be attempted and the delivery completed.

Summary

1. A five-year review is presented of 12,787 deliveries with 2,068 x-ray pelvimetric examinations, in which flat sacra were demonstrated.

2. Increased incidence of operative delivery is suggested in the flat-sacrum group.

3. Increased incidence of breech presentation was found in the flat-sacrum group.

4. Labor was prolonged in 40.2 per cent of the flat-sacrum group.

5. The problem of occiput transverse arrest in the midpelvis and the effect of the flat sacrum are discussed.

6. In a series of 440 patients with flat sacra, the cesarean section incidence was 17.7 per cent as contrasted to a cesarean section incidence of 4.9 per cent for all deliveries.

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THE EFFECT OF THE STAGE OF GESTATION AND NUMBER OF PREGNANCIES ON SUSCEPTIBILITY TO POLIOMYELITIS

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AMONG the many people who are exposed to poliomyelitis virus, the preponderant result of which is subclinical immunization, the more frequent occurrence of the frank disease under particular circumstances and in certain individuals is highly suggestive of mechanisms of susceptibility related to the character of the host rather than to the nature of the virus. Although previous exposure with the development of immunity plays a major role, there appear to be various nonspecific host factors which are determinants not only of susceptibility to viral invasion but probably also of the course and outcome of the disease once infection has occurred.

It has been suggested that variation in the frequency of clinical poliomyelitis, apparent and inapparent, is related to a number of factors among which are a distinctive constitutional type,[1, 2] heredity,[3] tonsillectomy,[4-11] fatigue,[12] antigen injections,[13-16] and pregnancy.[17-23] Although Bowers and Danforth[24] could not establish such a relationship, it is the consensus of medical opinion that pregnancy increases susceptibility to the development of clinical poliomyelitis. The most recent observations[19, 20] show that from 20 to 25 per cent of women in the childbearing age who have this disease are pregnant. In Massachusetts, approximately 7 per cent of healthy women in this age group are pregnant at any given time;[20] this is about one-third the rate observed in poliomyelitis patients and establishes the significance of gestation as a factor which increases susceptibility. In 140 women with "infantile paralysis," Bowers and Danforth[24] found 17 per cent to be pregnant and concluded that there was no relationship between the two. This report does not include, however, any data concerning normal women in the area in which the study was carried out.

Multigravidity and the duration of gestation may be of importance in increasing the heightened susceptibility to poliomyelitis associated with pregnancy. In a group of 70 gravid women who had "infantile paralysis" which Weaver and Steiner[25] collected from the literature, 17.1 per cent were in the first, 34.3 per cent in the second, and 48.6 per cent in the third trimester. In 428 patients observed by Bowers and Danforth,[24] poliomyelitis occurred least frequently in the third trimester. The effect of the number of pregnancies prior to the one in which poliomyelitis appeared on susceptibility to this disease has also been studied by Bowers and Danforth. In 24 cases which they observed personally, only 8.3 per cent of the patients were gravida i; in 84 others collected from the literature, however, 31.3 per cent were pregnant for the first time.

In view of the controversial observations concerning the influence of the duration of gestation and the number of pregnancies in conditioning susceptibility to poliomyelitis during pregnancy, the studies described in this paper were undertaken. It is the purpose of this report to present data which indicate that "infantile paralysis" occurs during pregnancy most often in the second trimester, although this is less evident in large groups, and that primigravid women are less susceptible than those who have had a least one pregnancy prior to the one complicated by infantile paralysis.

Methods

The 60 patients included in this study were observed at the Haynes Memorial Hospital (57 cases) and the Children's Medical Center (3 cases) from 1946 through 1953. All of them were pregnant and in the acute phase of poliomyelitis. In most instances, the data concerning previous pregnancies were obtained through personal interview at the bedside or by means of the telephone; in a few, review of the clinical charts yielded the necessary information. The duration of the pregnancy complicated by "infantile paralysis," the number and outcome of prior gestations, and the type of nervous system disease were ascertained.

In order to evaluate properly the data concerning the relationship of the number of pregnancies to susceptibility to poliomyelitis, information was secured from the Bureaus of Vital Statistics of the states of New York, Connecticut, and New Hampshire indicating the parity of women admitted for delivery in these areas; such statistics are not available in Massachusetts. These figures, which are presented in the following section, pertain to *multiparous* or *primiparous* rather than *multigravid* or *primigravid* patients.

Results

Relation of Duration of Pregnancy to Susceptibility to Poliomyelitis.— In the group of 60 pregnant patients with poliomyelitis, 14 (23.34 per cent) were in the first, 30 (50 per cent) in the second, and 16 (26.66 per cent) in the third trimester. As can be seen in Table I, the majority of those in each period of pregnancy (72 to 81 per cent) had the paralytic type of disease; although the incidence of paralysis was somewhat higher in the third than in the first trimester, this difference is probably of little statistical significance. When the patients were divided into groups on the basis of the month of pregnancy, vulnerability to the development of paralysis appeared to be greatest in the fifth and seventh months of gestation (Table II). Although the number of women in each group is small, it is interesting to analyze the relationship between the age of the patients and the trimester of pregnancy in which they appeared to be most susceptible to poliomyelitis. As can be seen in Table III, there was very little difference in the prevalence of poliomyelitis in the first two trimesters in the youngest age group (20 to 24 years) while in those aged 25 to 29 the disease occurred most often in the last 3 months. In women 30 to 36 years of age, poliomyelitis was most frequent in the last trimester; the data in this group confirm the observations of Weaver and Steiner.[25] These findings suggest that age may be an important factor in determining susceptibility to poliomyelitis in various trimesters of pregnancy and that studies of the effect of the duration of gestation on the incidence of this disease may yield different results unless the age distribution of the patients is taken into consideration.

Table IV presents a summary of the data on 543 patients collected from the literature,[24, 25] together with the cases reported in this paper, without reference to age. In this relatively large group, very little difference is apparent in

various trimesters of gestation. The prevalence of poliomyelitis in the first and last three months is identical. A small increase is apparent in the second trimester, however; this is only 8 per cent more than in the other two periods and may be of little importance. In large groups of pregnant women, therefore, the duration of gestation seems to play little role in determining susceptibility to poliomyelitis, although in general the disease tends to occur somewhat more often during the second trimester.

TABLE I. RELATION OF DURATION OF PREGNANCY TO POLIOMYELITIS

AGE OF PATIENTS (YEARS)	FIRST TRIMESTER		SECOND TRIMESTER		THIRD TRIMESTER	
	NON-PARALYTIC	PARALYTIC	NON-PARALYTIC	PARALYTIC	NON-PARALYTIC	PARALYTIC
20-24	1	3	3	7	1	3
25-29	1	5	5	9	–	6
30-36	1	3	1	5	1	5
Total	14 or 23.34%		30 or 50%		16 or 26.66%	
Per cent paralyzed	72		77		81	

TABLE II. RELATION OF MONTH OF GESTATION TO TYPE OF POLIOMYELITIS

TYPE OF POLIOMYELITIS	DURATION OF PREGNANCY IN MONTHS							
	2	3	4	5	6	7	8	9
Paralytic	6	5	3	12	7	7	3	4
Nonparalytic	1	2	5	0	3	0	0	2

TABLE III. RELATION OF AGE TO SUSCEPTIBILITY TO POLIOMYELITIS IN VARIOUS TRIMESTERS OF PREGNANCY

TRIMESTER OF PREGNANCY	AGE GROUPS					
	20-24 YEARS		25-29 YEARS		30-36 YEARS	
	NO.	%	NO.	%	NO.	%
First	4	22.2	6	23.1	4	25.
Second	10	55.6	14	53.8	6	37.5
Third	4	22.2	6	23.1	6	37.5
Totals	18	100	26	100	16	100

TABLE IV. RELATION OF TRIMESTER OF PREGNANCY TO SUSCEPTIBILITY TO POLIOMYELITIS
Summary of Data in Literature and Present Cases.

TRIMESTER OF PREGNANCY	INVESTIGATORS AND NUMBER OF PATIENTS				
	WEAVER AND STEINER[25]	BOWERS AND DANFORTH[24]	WEINSTEIN AND MEADE	TOTAL	
				NO.	%
First	12	141	14	167	30.72
Second	24	154	30	208	38.98
Third	34	118	16	168	30.90
Total	70	413	60	543	100

The Relation of Number of Pregnancies to Susceptibility to Poliomyelitis.— In the group of 60 patients reported in this paper, the largest number were multigravid at the time they developed poliomyelitis. Only 6.67 per cent were gravida i when seen with "infantile paralysis"; 93.33 per cent had been pregnant before and these were about equally divided between patients who had had one previous gestation and those who were gravida iii or more when they came under our observation (Table V). These data are in close agreement with those of Bowers and Danforth[24] for the Evanston Hospital but are quite different from those collected by them from the literature.

TABLE V. RELATION OF NUMBER OF PREGNANCIES TO SUSCEPTIBILITY TO POLIOMYELITIS

GRAVIDITY	TOTAL PATIENTS		PARALYZED		AGE GROUPS (YEARS) 20-24		25-29		30-36	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
i	4	6.67	3	75	3	16.6	1	3.85	–	–
ii	27	45	22	88.4	12	66.7	14	49.9	1	6.25
iii or more	29	48.33	21	75.3	3	16.6	11	42.25	15	93.75
Total					18	100	26	100	16	100

In order to evaluate accurately the influence of gravidity on susceptibility to poliomyelitis, it is necessary to obtain information concerning the distribution of primigravid and multigravid individuals in the healthy pregnant population. The numbers of *primiparous* and *multiparous* women in the states of New York, Connecticut, and New Hampshire were ascertained from the Bureaus of Vital Statistics of these areas; such information was not available in Massachusetts. It must be stressed that the figures presented in Table VI represent *parity* and not *gravidity;* to use them, therefore, may be somewhat misleading because it is not known how many of the individuals had been pregnant one or more times before delivering a living child. Since no data concerning multigravid or primigravid women in the general population were available to us, parity had to be used as the point of reference. A summation of all of the patients in the three states from which information was secured showed that, of 353,180 pregnant women, 33.3 per cent were primiparous. When this is compared to 6.66 per cent and 8.3 per cent primigravid patients in the present series and in the one from the Evanston Hospital, respectively, it is apparent that the number of primigravid women with poliomyelitis was from one-fourth to one-fifth as high as the number of primiparous women in the healthy pregnant population.

TABLE VI. DELIVERIES IN PRIMIPAROUS AND MULTIPAROUS PATIENTS IN THREE EASTERN STATES

STATE	353,180 PREGNANT WOMEN			
	PRIMIPAROUS		MULTIPAROUS	
	NO.	%	NO.	%
New York	109,381	36.3	191,662	63.7
Connecticut	14,006	34.5	26,614	65.5
New Hampshire	3,331	29	8,186	71
Total	126,718	33.3	226,462	66.6

The occurrence of paralysis appeared to be related in some degree to the number of gestations preceding the one in which poliomyelitis developed. As can be seen in Table V, there were 13 per cent more paralytic cases of the disease in gravida ii patients than in those who were gravida iii; this is a relatively small difference and may not be significant.

Examination of the data which relate age to the number of pregnancies experienced prior to the one in which poliomyelitis occurred revealed some interesting differences; any conclusions, however, must be qualified by the fact that the number of patients in each group is rather small. In those 20 to 24 years old, most were gravida ii; in patients with poliomyelitis who were 25 to 29 years of age, the disease appeared most often in those who were multigravid but little difference was detectable in the groups pregnant only twice and those who had had three or more gestations. Most striking is the very high prevalence of "infantile paralysis" (93.75 per cent) in individuals between 30 and 36 years of age who were multigravid when they became ill with this infection. These data must be analyzed, however, in terms of the percentage of women who were 30 to 36 years old in the entire group of those who had been pregnant three or

more times. As can be seen in Table VII, most of the patients aged 20 to 24 were pregnant for the first time, those 25 to 29 years old had had one previous pregnancy in most instances, and more than half of the oldest individuals were gravida iii or more. This distribution is to be expected because the older age groups had been married for 5 to 15 years longer than the younger ones. A comparison of the data for gravida iii in Table VII with those for the same group in Table V reveals that, although the number of pregnancies increased with age, there were almost twice as many cases of poliomyelitis (93.75 per cent) in those aged 30 to 36 who had been pregnant three or more times than there were gravida iii patients in all age groups combined (51.8 per cent of all the gravida iii women were 30 to 36 years old). This observation suggests that the high frequency of poliomyelitis in gravida iii patients is not due to age alone but results from the impact of both age and multiple pregnancies.

TABLE VII. RELATION OF AGE TO NUMBER OF PREGNANCIES

	AGE GROUP (YEARS)						TOTAL	
	20-24		25-29		30-36			
GRAVIDITY	NO.	%	NO.	%	NO.	%	NO.	%
i	3	75	1	25	–	–	4	100
ii	12	44.4	14	51.8	1	3.8	27	100
iii or more	3	10.32	11	37.84	15	51.84	29	100

Since the two sets of observations of Bowers and Danforth (cases collected from the literature and those studied at the Evanston Hospital) are not in agreement, and the data obtained by us are also not in accord, it is interesting to combine all of the cases and to determine whether there is the same correlation between number of pregnancies and susceptibility to poliomyelitis in this large group as there is in the smaller ones. If the patients from the Evanston Hospital are added to ours, the number, 84, is identical with that collected from the literature by Bowers and Danforth. A comparison of these two groups (84 each) is presented in Table VIII; the discrepancy is striking. Since the women in the Evanston and Haynes Memorial Hospitals were observed personally by Bowers and Danforth and by us, the question may be raised as to possibility of error in the recording of gravidity in reports collected from the literature as the cause of the difference in results. An analysis of all of the reported cases, a total of 168, shows that, even in this large number, poliomyelitis occurred most often in multigravid women; 81 per cent of the patients were in this group; this is 15 per cent higher than could be expected on the basis of prevalence of multigravidity in the healthy pregnant population.

TABLE VIII. RELATION OF NUMBER OF PREGNANCIES TO SUSCEPTIBILITY TO POLIOMYELITIS ALL RECORDED CASES

	CASES FROM LITERATURE BOWERS AND DANFORTH[24]		SUM OF EVANSTON[24] AND PRESENT CASES		SUM OF THREE SERIES OF CASES	
GRAVIDITY	NO.	%	NO.	%	NO.	%
i	26	31.3	6	7.1	32	19.1
ii	35	42.2	40	47.6	75	44.6
iii or more	23	26.5	38	45.3	61	36.3
Total	84	100	84	100	168	100

Summary and Comment

A study of 60 patients who had poliomyelitis during pregnancy indicates that this disease appears most often in the second trimester. Bowers and Danforth found only a small variation in susceptibility between the second and third trimesters; Weaver and Steiner showed that the prevalence of poliomyelitis was

highest in the last three months of gestation. When all of the reported cases are grouped together, a total of 413, the largest number of individuals is found to be in the second trimester; the difference is only 8 per cent and may be of little or no significance.

Analysis of the data obtained in the present study on the basis of age of the patients indicates a definite predisposition to the development of poliomyelitis in the second trimester in those 20 to 29 years old, there being about two and one-half times as many cases in the second as there were in the first or last trimester; in the older individuals, aged 30 to 36 years, the difference is small and is probably not significant. The number of patients included in the present study is relatively small and, for this reason, it is difficult to draw any definite conclusions. It appears, however, that the stage of gestation plays some role in increasing susceptibility to poliomyelitis in young women but is probably of little importance in older ones. There are no data available concerning the age distribution of patients in other reported studies[24, 25]; if these were available, some of the observed discrepancies might be much less apparent.

Studies of the influence of the number of pregnancies experienced by a patient prior to the one in which poliomyelitis developed indicate that primigravid individuals have this disease much less frequently than multigravid ones. Although one series of cases[24] contained a number of multigravid women no greater than is thought to be present in the healthy pregnant population, this group was composed of reports collected from the medical literature. In our own group and in those observed personally by Bowers and Danforth, the increased prevalence of poliomyelitis in those who had had more than one gestation is almost identical. Analysis of the total number of cases, 168, discloses almost 15 per cent fewer primigravid women with poliomyelitis than there are instances of first gestation in normal women; the ratio of multigravidity to primigravidity in poliomyelitis is 4:1 while in healthy women it is 2:1.

Although the number of cases in the present study is small, an analysis of the age distribution suggests that the prevalence of poliomyelitis is highest in older multigravid women, aged 30 to 36; this is so despite the larger number of patients who have had more than one pregnancy in this group.

The development of paralytic or nonparalytic poliomyelitis appeared to be influenced to a small degree by the number of pregnancies; muscle weakness was more common when the disease occurred during certain months of gestation. Whether or not pregnant women have a more severe type of poliomyelitis than nonpregnant ones in the same age group has been determined by Anderson[19] whose figures, corrected for age and incidence of paralysis among nonpregnant women of the same age group, show no difference. The heightened susceptibility to poliomyelitis during pregnancy does not, therefore, indicate an altered vulnerability to the effects of the virus once infection has taken place. Parturition occurring the acute phase of the disease does, however, increase the risk of extensive paralysis in many instances. Anderson has suggested that specific months of pregnancy may be associated with a high frequency of paralytic involvement; the second and fifth months were the most dangerous. In the present series, 100 per cent of the patients in the fifth and seventh months of gestation were paralyzed.

The mechanism of the increased susceptibility to poliomyelitis associated with multigravidity is not apparent. The possibility suggests itself that multiparous women may be exposed more often and to a greater degree to the disease because they are in close contact at home with children who may have the infection or who are asymptomatic carriers of the virus. This remains to be proved. The data presented in this paper, while highly suggestive of an increased susceptibility to poliomyelitis related to the duration of gestation and the number of pregnancies which have been experienced, are not conclusive because of the relatively small number of patients studied. This problem merits further investigation since it indicates that there may be factors characteristics of the host which exert an important effect in further altering the state of decreased resistance to poliomyelitis usually associated with pregnancy.

Conclusions

1. Poliomyelitis tends to occur with somewhat greater frequency in pregnant women during the second trimester, especially in young individuals.

2. The paralytic type of poliomyelitis develops most often in the fifth and seventh months of gestation.

3. Multigravid women appear to be more susceptible to poliomyelitis; paralysis was present most often in gravida ii patients in the present study.

4. Older age seems to accentuate the increased susceptibility to poliomyelitis associated with multigravidity.

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PREGNANCY COMPLICATED BY COCCIDIOIDOMYCOSIS: REPORT OF TWO CASES*

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COCCIDIOIDOMYCOSIS is an infection caused by the fungus, *Coccidioides immitis*. The disease was first reported by Pasadas and Wernicke in South America.[1] In the United States the first case reported, by Rixford in 1894, was that of a patient in the San Joaquin Valley of California.[1] The principal endemic foci are located in the southern part of the San Joaquin Valley of California, Southern Arizona, and Western Texas.[1]

The fungus is grouped with the *Fungi imperfecti*. It exists outside its host in the form of spores and mycelia which become chlamydospores and, after entry into man or animals, mature into spherules and endospores.[2]

Man becomes infected through inhalation of the chlamydospores present in dust-laden air.[1] Infection may occur merely as the result of travel by auto or train through areas of endemic foci. This is usually during the dry summer and fall months.[1] The spores also may be transported in clothing or dusty products shipped from or through the endemic area.[3]

Males and the dark-skinned races are more susceptible to the disease and to dissemination.[1] The latter is ten times more likely to occur in the dark-skinned.[4] Meningeal dissemination, however, occurs more often in white rather than in colored males.[4] White races are more likely to have the acute form while darker races are more susceptible to the progressive form.[5] Females predominantly have the acute form, while more males develop granulomas. There is an approximately even distribution between males and females under age 13 and over 60, but more males in the age group 14 to 60.[6]

The incubation period is from 8 days to 3 weeks, usually 10 to 14 days.[5] In tissue the fungus causes a granulomatous reaction with a tendency to central caseation and suppuration.[1] The disease occurs in two forms: (1) primary coccidioidomycosis which is an acute, benign, self-limited, respiratory infection, and (2) progressive coccidioidomycosis which is a chronic, disseminated, and usually fatal disease characterized by cutaneous, subcutaneous, visceral, or osseous lesions.[1]

Dissemination occurs in a ratio of 1 in 500 cases.[7] The mortality rate is approximately 50 per cent in the progressive form.[7] The most common sites of dissemination are the skin, subcutaneous tissue, lymph nodes, lungs, bones, meninges, joints, peritoneum, and the liver.[2] The gastrointestinal tract is im-

*The opinions expressed are those of the author and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

mune to this disease.[7] Dissemination may occur as late as 10 years after the primary infection.[8] Of residents of endemic areas for 10 years or more, 75 per cent will have positive coccidioidin skin tests.[1]

The disease is usually not recognized in its primary form, being diagnosed as a common cold, bronchitis, pneumonia, influenza, or as having no clinical symptoms or signs.[1, 2] Sixty per cent of cases may be asymptomatic.[3, 9] In recognized cases the symptoms are those of pneumonitis, usually with hilar node enlargement, the primary focus nearly always undergoing some degree of cavitation.[1] X-rays of the chest will demonstrate inflammatory changes in 80 per cent of the cases.[7] The most frequent, and usually the predominant symptom is thoracic pain occurring in 75 to 80 per cent of patients who have symptoms.[10] The chest pain as a rule is substernal or pleuritic.[2] A cough is usually present and may be nonproductive and brassy or slightly productive of mucopurulent to blood-streaked sputum.[1] Hemoptysis is uncommon, but it may occur with residual cavitation.[10] The temperature is usually low grade to 101° F.,[1] but may rise from 101 to 103° F.[2] The respiratory and pulse rates follow the degree of fever. Chills, malaise, anorexia, headache, backache, night sweats, and transient arthralgia may be present.[1, 2] The arthralgia is not relieved by salicylates.[1, 7] Allergic symptoms such as erythema nodosum or erythema multiforme occur in 5 per cent of the cases.[2] Females may demonstrate allergic manifestations in as many as 25 per cent of the cases.[9] Urticaria may be an allergic sign[3] and the eosinophil count is usually high.[2, 9] The erythrocyte sedimentation rate is elevated and there may be a leukocytosis with a shift to the left on the differential.[2] Pleural effusion also may be seen.[1] After one to two weeks the fever abates and the cough and chest pain disappear, but 3 per cent of recognized cases may have a secondary phase in 3 to 21 days with a recurrence of fever and allergic manifestations.[1, 2]

The patients with erythema nodosum and erythema multiforme are least likely to have dissemination.[1] Chest x-rays disclose a variety of findings.[2] There is usually pneumonitis with hilar adenopathy, but lobar, miliary, or nodular consolidation may occur. Cavitation is generally small and thin walled, and may persist for months. Later, one may find calcific residue of single or multiple areas. Pleural effusion is usually minimal and the cavitation customarily clears rapidly.[4] Cavitation may occur in a residual lesion many months after the initial symptoms.[11] Dissemination rarely occurs in patients with cavities, probably because they possess an effective immunity mechanism.[11]

Diagnosis depends upon awareness and recognition of symptoms. X-rays of the chest are very helpful. Coccidioidin skin testing is used extensively and is very valuable. Precipitin tests rise early in the primary infection and fall at the time of rise of the complement fixation antibodies.[4] The complement fixation indicates active or progressive disease while the precipitin test indicates recent infection.[12] The longer the coccidioidin skin test remains positive the better the prognosis.[12] The most accurate procedures for diagnosis are demonstration of the organism by direct mount, culture, or animal inoculation, but these are difficult and dangerous.[4] The course of the disease can be followed with the serologic tests after clinical signs and symptoms have abated. Cavitation and

other x-ray findings should be followed by serial roentgenography. The erythrocyte sedimentation rate is a good index of remission or progression of the disease.

There is no specific treatment at the present time for combating this disease.[7] Usually no therapy is required other than bed rest and relief of symptoms. Occasionally pneumothorax must be resorted to for control of hemorrhage from cavitation.[4] Hematologic and serologic studies return to normal except for an iron-deficiency anemia.[1]

There are no known cases wherein the disease has been transmitted from one individual to another,[12] but one author believed that infection in man should be considered as contagious and he has shown that it can be transmitted from man to experimental animals.[13]

Warning signs of impending dissemination are persistent symptoms, high erythrocyte sedimentation rate, and a rising complement fixation titer.[12] There is strong evidence that dissemination practically always occurs relatively soon, that is, within a few months after the initial infection.[12] Dissemination is least likely in white females except during the last trimester of pregnancy.[9]

In progressive coccidioidomycosis the fungus disseminates throughout the body in a manner similar to miliary tuberculosis.[1] The primary stage is followed within a few weeks or months by a recurrence of symptoms similar to those originally experienced. The erythrocyte sedimentation rate is increased as is the complement fixation titer. The fever becomes high and emaciation results. Large subcutaneous abscesses, arthritis, cystic degeneration of bone, and meningitis may occur along with caseation necrosis of any other part of the body involved. X-rays reveal further evidence of lung infiltration and may indicate involvement of other organs, such as bone, joints, lymph nodes, etc. If pulmonary pathosis predominates, death is due to anoxia after a prolonged course of many weeks to six months, as a rule.[1] A profound anemia is characteristic.[8] Localization in the meninges characteristically produces a basilar meningitis[3, 5] and often leads to hydrocephalus.[5]

A patient with coccidioidal meningitis presents a problem of differential diagnosis when no other lesions are present. The diagnostic possibilities embrace such diseases as brain tumor, degenerative diseases of the brain, infectious intracranial lesions such as brain abscess, viral encephalitis, neurosyphilis, tubercular meningitis, or other central nervous system infections, bacterial, protozoan, or fungus. Coccidioidomeningitis is of two essential varieties.[8] One type is a firm, plastic meningeal inflammation which results in a granulomatous encasement of the brain, particularly the brain stem, in a rigid, highly organized mass of tissue. The second type is characterized by a pronounced exudation of fluid with minimal granulomatous transformation. Extreme grades of hydrocephalus can occur with the first type. Abnormalities of the spinal fluid characteristically suggest the possibility of coccidioidal meningitis. The spinal fluid protein is markedly elevated, spinal fluid sugar tends to be low, and a paretic type of gold curve is seen.[3] The cell count is variable, but commonly contains polymorphonuclear leukocytes and some may have mostly lymphocytes.[5] The spinal fluid leukocytes may contain a proportionately high number of eosinophils. The spherules are rarely found in the spinal fluid with meningitis,[5] and the

organism is difficult to culture from spinal fluid.[3] A conclusive diagnosis can be made on significant amounts of complement fixation antibodies in the spinal fluid. Usually the coccidioidin skin test is positive and the complement fixation titer or precipitin test may be high.[3]

The first reported cases of disseminated coccidioidomycosis as a cause of maternal death in pregnancy was reported by Smale and Birsner[14] in 1949 in an analysis of 4 maternal deaths out of 2,410 deliveries for the year 1948 at the California Kern General Hospital. Three of these were due to disseminated coccidioidomycosis. In these cases, there was absence of the disease in the generative tract although they mentioned knowledge of a case of placental granulomas from coccidioidomycosis. Vaughan and Ramirez[15] reported 33 cases of coccidioidomycosis in pregnancy from 1942 to 1949 from the physicians' and hospital records of Kern County, California. The authors were impressed by the rapidity of generalized dissemination of the disease when it occurred in the last trimester of pregnancy. Of 5 cases in which the disease preceded pregnancy, 1 patient aborted spontaneously, 2 others threatened to abort, 1 received a therapeutic abortion because of pulmonary hemorrhage, and the remaining case was uncomplicated. There were 11 cases of the disease in the third trimester, 6 in Caucasians, 4 in Negroes, and 1 in a Chinese. Four of the cases in Caucasians were uncomplicated, the other 2 having a generalized disease and delivering premature viable infants. The Chinese patient's disease also became generalized and she delivered a viable, premature infant. All four of the Negroes developed dissemination; 2 delivered prematurely viable infants, one a stillborn, and one died undelivered. In none of these cases were the infants infected, but one placenta revealed multiple areas of invasion by spherules.

Following are two case reports of coccidioidomycosis during pregnancy at the United States Naval Hospital, Oakland, California. These are the only cases during pregnancy seen at this hospital over a period of 11 years from August, 1943, to August, 1954, when approximately 24,700 deliveries were performed.

Case Reports

CASE 1.—M. T., a 17-year-old white woman, gravida i, para 0, stated that her last normal menstrual period was six weeks prior to the time she was first seen here, and that she had lived in an area 100 miles south of Fresno, California, from the age of 13 until January, 1954. During the last week of October, 1953, she developed a pleuritic pain, cough, generalized aching, malaise, anorexia, and fever to 101° F. Two weeks later she developed erythema nodosum of both legs. A coccidioidin skin test was positive. X-ray of the chest revealed infiltration in the mid-portion of the left lung. She was asymptomatic except for a moderate degree of iron-deficiency anemia by December, 1953.

On her first visit to this hospital, March 18, 1954, the history and physical examination showed no evidence of progression of the disease. The coccidioidin skin test was positive at a 1:100 dilution. Complement fixation and precipitin tests were negative. X-ray examination of the chest showed an area of increased density at the level of the anterior end of the third rib on the left. The Aschheim-Zondek test was positive. Other laboratory data, such as the Kahn test, antistreptolysin titers, blood and urine studies, were within the limits of normal.

On May 1, 1954, she began to bleed per vaginam and spontaneously aborted on May 6. Dilatation and curettage were done on May 10. Pathologic examination of the products of conception, both that which was passed spontaneously and that which was obtained from the curettage, showed no evidence of coccidioidomycosis.

Follow-up serologic and x-ray studies did not produce evidence of dissemination.

Case 2.—L. R., a 32-year-old white woman, gravida iv, para iii, whose estimated date of confinement was March 12, 1953, was admitted to this hospital in labor on March 9, 1953. Her prenatal course had been essentially normal until two weeks prior to admission. She gave a history of having had the "flu" for the previous two weeks with severe, shaking chills, fever, myalgia, headache, and stiff neck. Later, upon checking with her neighbors, it was found they had noticed lethargy, despondency, and had commented on the exquisiteness of her headaches; also that she had complained of numbness of the left arm. On March 4 a doctor had taken her temperature, stating that it was 102° F. and on examination had believed the disease to be an upper respiratory infection and had given penicillin and Terramycin. The patient's parents related that in 1949, after delivery, she had fainting spells and with one syncope one pupil was larger than the other. Also, one year previously the patient's small dog had died of something contagious at Ord Grove, California, and they were told by the veterinarian to burn the dog, its bedding, and the doghouse, and that the small children should not go near the area. They acquired another dog which later died in a dog hospital of pneumonia.

At the time of her admission to this hospital the patient was found to be in labor with a viable term pregnancy. Physical examination disclosed no heart or lung pathosis and neurological findings were normal. Four hours later she delivered, by low forceps under pudendal block anesthesia, a viable male infant. The mother was noted to be "bland" in her reaction to delivery and to her infant. One and one-quarter hours post partum the nurse noted the patient did not comprehend simple commands but believed this to be due to sedation. At two and one-half hours post partum the nurse noted facial asymmetry and called the ward medical officer. Examination showed left hemiparesis in a patient who was confused and disoriented but answered questions coherently although slowly. She was thought to have had a middle cerebral vascular accident on the right or possibly a diffuse encephalomeningitic process. Examination of spinal fluid showed a manometric reading of 220 mm. of water; 660 white blood cells with 98 per cent lymphocytes and 100 red blood cells. Spinal fluid sugar was 25 mg. per cent, total protein 77.6 mg. per cent, chlorides 670 mg. per cent, with a positive Pandy reaction. A culture and stained smear of the sediment were negative.

Many possibilities of diagnosis were entertained and a large variety of tests were performed, but yielded no further information.

The neurologists believed the patient to have either thrombosis or embolus of the right middle cerebral artery although an infectious process could not be ruled out. She was treated with penicillin, streptomycin, and later sulfonamides in an attempt to eradicate infection if it existed.

The patient rapidly became comatose with a high fever and more marked neurological findings, finally requiring tracheotomy and continuous oxygen therapy over and above general supportive measures. She died on the ninth day of hospitalization.

An autopsy revealed chronic coccidioidal meningitis, basilar type, chronic coccidioidal encephalitis, and coccidioidal pneumonitis. A thorough study of the generative organs and the placenta showed no evidence of invasion. The delivered infant demonstrated no indications of coccidioidomycosis but was removed from this area by its grandparents before a complete follow-up could be effected.

Summary

Presented is a condensed general discussion of coccidioidomycosis, relating particularly to coccidioidomeningitis and coccidioidomycosis in pregnancy. In the 11 years of operation of the United States Naval Hospital, Oakland, California, approximately 24,700 deliveries have been performed. There have

been only 2 cases of coccidioidomycosis in pregnancy. One case became apparent in the last trimester of pregnancy, ending fatally with coccidioidomeningitis. The other case was that of early pregnancy with a recent infection of coccidioidomycosis, demonstrating positive findings in the lungs and ending in spontaneous abortion.

These cases are presented to substantiate previously reported instances of this disease during pregnancy and the conclusions drawn from them.

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PREGNANCY WITH A RECURRENT GRANULOSA-CELL TUMOR

Report of Case and Review of Literature on Granulosa-Cell Tumors Complicating Pregnancy

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THE granulosa-cell tumor is one of the group of feminizing ovarian tumors. Interest in this lesion is evidenced by the fact that more than 900 cases of this tumor have been reported. It is commonly accepted that the presence of this neoplasm induces temporary sterility that is reversible by extirpation of the growth. Pregnancy after removal of such a tumor has been reported frequently. Coexistence of pregnancy and a granulosa-cell tumor is decidedly unusual, however, only 15 such cases having been reported in the world literature.[1-15] It was considered worth while, therefore, to record the first case in which pregnancy was concomitant with a *recurrent* granulosa-cell tumor.

Report of Case

A 37-year-old, white, married nulligravida first registered at the Mayo Clinic in June, 1953. She had been well up to 1948. At that time her menses, previously regular, gradually diminished in frequency over a period of 4 or 5 months, after which the flow stopped completely for 18 to 24 months. A tumor was then discovered low in the right side of the abdomen. Laparotomy elsewhere disclosed a granulosa-cell tumor originating from the right ovary (Fig. 1, *a* and *b*). Right salpingo-oophorectomy was done. Her periods then resumed a normal pattern and continued so until June, 1952, when amenorrhea recurred. A second laparotomy elsewhere in October, 1952, revealed "6 pelvic tumors," which were removed.

The patient then improved until 2 months prior to registration at the clinic when, following a period of amenorrhea since October, 1952, she had two episodes of gushing vaginal bleeding, with intermittent and severe abdominal cramping. She had lost 6 pounds during the previous 6 months.

Abdominal examination at the clinic disclosed a mass in the left lower quadrant that was ovoid, soft, and moderately tender; it measured about 4 by 10 cm. Bimanual examination showed it to be probably cystic; the adnexal mass could not be distinguished with certainty from the corpus uteri. A few scattered nodules were palpated in the right cul-de-sac, and a firm mass measuring 2 by 2 by 3 cm. was noted in the right broad ligament. Results of rectal examination were negative. Both breasts exhibited great nodularity.

The erythrocytic sedimentation rate was 58 mm. during the first hour (Westergren). Results of other laboratory tests were within normal limits. Hormonal studies were not done. Roentgenograms of the thorax and abdomen disclosed nothing abnormal.

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*The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

Surgical exploration was performed 5 days after admission, with the preoperative diagnosis of recurrent granulosa-cell carcinoma. The large central mass arising out of the pelvis, which had felt somewhat cystic, proved to be the fundus of the uterus. The latter was soft and appeared much like the uterus seen in pregnancy. Old hemorrhagic fluid was encysted behind the uterus and the sigmoid and omentum were loosely adherent to the fundus. On separation of these adhesions, a tumor 6 cm. in diameter was found in the right posterior uterine wall. This tumor also was adherent to the large intestine and to the pelvic wall. Numerous small nodules of tumor were noted also in the left gutter and in the fatty fringe of omentum near the uterus. Study of fresh frozen sec-

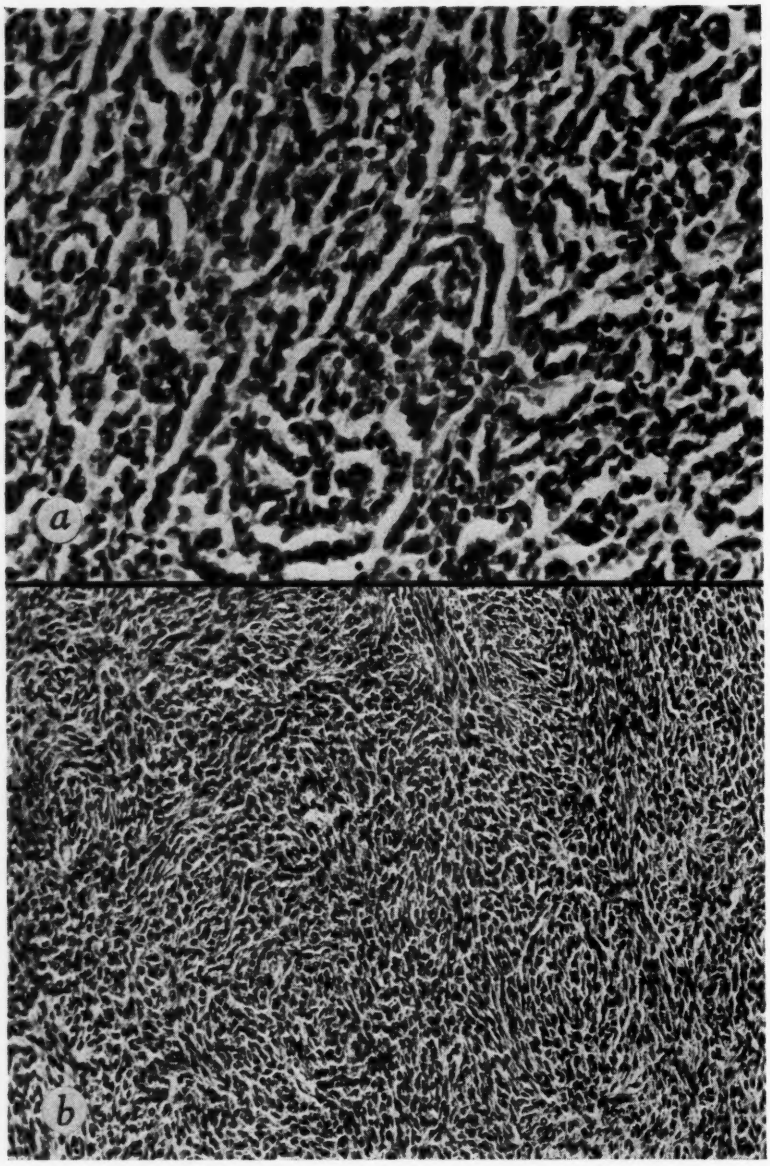

Fig. 1.—The original granulosa-cell tumor in this case. *a*, Note the typical moiré-silk variant of the cylindroid pattern. (Hematoxylin and eosin; ×300.) *b*, Note the predominantly diffuse or sarcomatoid pattern; mitotic figures were easily found in these areas. (Hematoxylin and eosin; ×160.) (This material was obtained through the courtesy of Dr. D. F. Mullins, Jr., Department of Pathology, Medical College of Georgia, Augusta, Ga.)

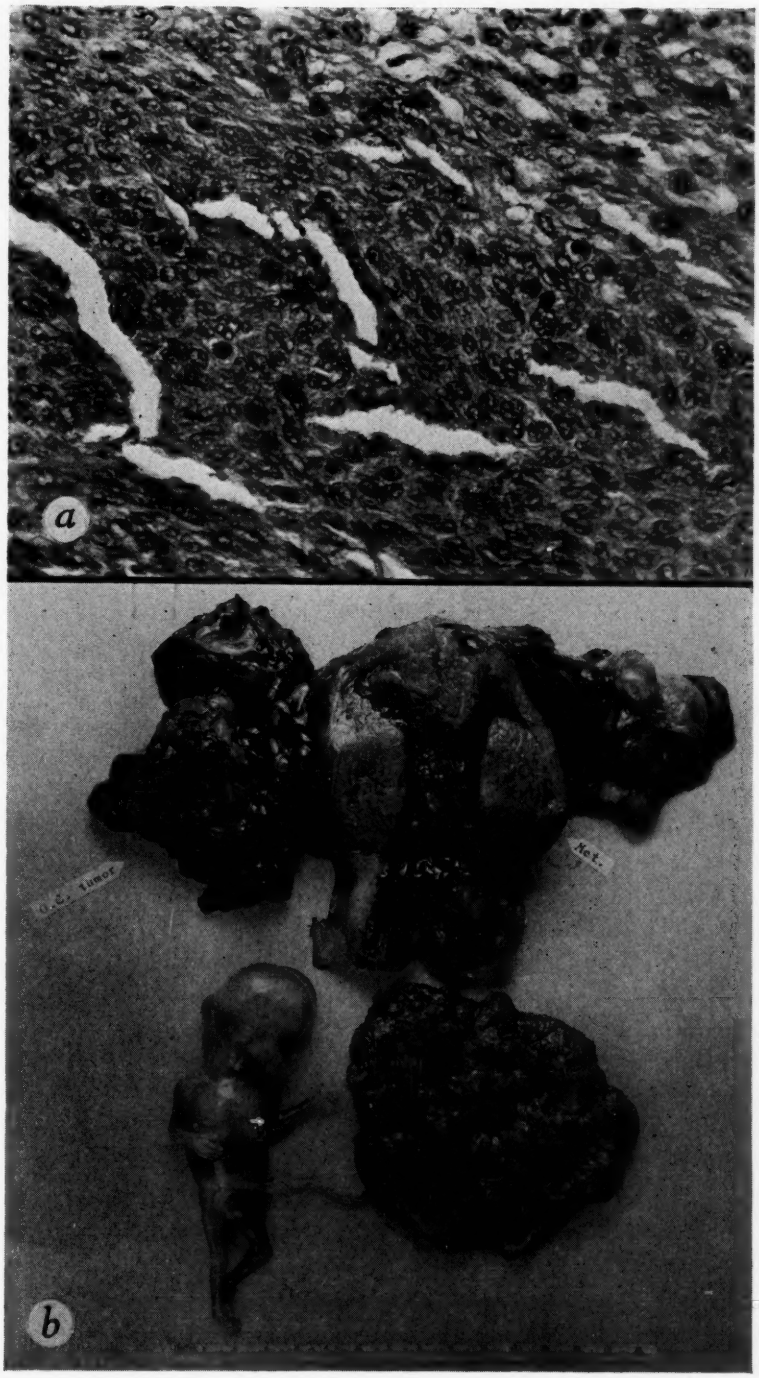

Fig. 2.—*a*, Recurrent granulosa-cell carcinoma. The tumor, which is predominantly sarcomatoid in pattern, exhibits numerous mitotic figures. (Hematoxylin and eosin; ×330.) *b*, Recurrent granulosa-cell carcinoma in both adnexal areas, more extensive on the right. A metastatic nodule is present on the surface of the uterus. The fetus is 10 cm. in length.

tions of an excised nodule revealed recurrent granulosa-cell carcinoma. The fringes of omentum were excised, along with all visible metastatic lesions. A normal-appearing left tube and ovary were identifiable when the adhesions about the uterus were freed. A total hysterectomy and left salpingo-oophorectomy were done, with removal of the large tumor in the right posterior uterine wall. The latter was fairly easily shelled off the large intestine, as it appeared to be pushing on the surrounding organs rather than invading them. After removal of the uterine mass one could observe numerous small tumor nodules, 2 to 5 mm. in diameter, so scattered throughout the pelvic peritoneum that it was not possible to remove all of them. The vaginal vault and abdomen were closed without drainage. The patient's postoperative course was uncomplicated.

The specimen consisted of the uterus, left tube and ovary, a portion of omentum, and the large recurrent tumor from the right side of the pelvis. The aggregate weight was 470 grams. The recurrent tumor was a granulosa-cell tumor of Grade 2 malignancy (Fig. 2, *a*) forming a mass 8 cm. in diameter. There was metastasis to the back of the uterus, left tube and left ovary (Fig. 2, *b*), with nodular spread to the omentum. The uterus contained a 10 cm. fetus.

After operation, roentgen therapy was given to the pelvis, a tumor dose of 3,080 r being delivered to the midpelvic plane in 26 days.

The patient returned for examination 1 year after operation, at which time she had no complaints referable to the pelvis. No evidence of recurrent tumor was noted.

Comment

We have subdivided the reported cases into three categories, namely (1) acceptable cases, (2) questionably acceptable cases, and (3) "cited instances." Questionably acceptable cases consisted of full case reports without photomicrographs. The cases falling into the first two groups are summarized in Table I.

The "cited instances" were mere notations, usually not more than one or two sentences in length. We have included 5 cases in this category. Szathmáry,[11] in 1932, noted a granulosa-cell tumor removed at term, when it had been an obstacle to delivery. In 1940, Gerundo[12] mentioned a young woman who was pregnant when such a tumor was discovered. She later had a normal labor. Folsome[13] mentioned a case in which pregnancy and a granulosa-cell tumor were associated. In 1949, Hamilton and Higgins[14] reported on a 38-year-old woman, para 0 and gravida i, from whom a granulosa-cell tumor measuring 8 by 11 cm. was removed at the sixteenth week of pregnancy. Delivery of a male child occurred at term. Finally, Strother[15] stated that part of a granulosa-cell tumor was removed from a patient after rapid abdominal enlargement was noted early in pregnancy, which went to term. A second pregnancy, 2 years later, ended spontaneously at 6 months after premature rupture of the membranes.

A case report by Kusuda,[16] frequently mentioned, is not included since he was not dealing with a granulosa-cell tumor. Robinson[17] reported a case in which a granulosa-cell tumor of the right ovary measuring 7 by 4 by 5 cm. had been removed 4 months after termination of a pregnancy at the seventh month for continuous uterine bleeding. We are not including this case inasmuch as there was not positive proof of the concomitance of the 2 conditions.

It is unfortunate that in none of these cases, including our own, were hormonal studies done on the urine, blood, or tumor tissue. In general, the number of hormonal studies carried out in cases of granulosa-cell tumor is disappointingly few.

The rarity of intrauterine pregnancy in association with a granulosa-cell tumor has been stressed by many authors. The basis for this rarity undoubtedly lies in suppression of ovulation. This is most likely due to the combination of pituitary inhibition and suppression of the remaining normal ovarian tissue by the increase in circulating estrogenic substance. For ovulation and subsequent pregnancy to take place in the presence of this neoplasm we believe that there must be a fluctuation in the level of circulating estrogens or else the tumor must produce but a small amount of estrogenic substance. One of us (Dockerty[18]) has said that pregnancy can occur in the presence of small granulosa-cell tumors. This is evidenced by Henderson's[4] case, in which a microscopic tumor was found incidentally at the time of therapeutic abortion. A small tumor may give but little estrogenic effect. Large granulosa-cell tumors may be associated with pregnancy, however.[1, 3,5-8, 10] Therefore, after reviewing the reports, we believe that levels of hormones are not dependent on the size or histologic pattern of the growth, though the more undifferentiated tumors probably produce less estrogenic substance; this concept must await further proof. We were impressed by the number of cases reported in which there were no signs or symptoms attributable to hormonal effects; more than two-thirds of the tumors were without obvious estrogenic effect.

Another feature worthy of comment in our case is the presence of a malignant granulosa-cell tumor in a young woman. One of us (Dockerty[18]) noted previously that recurrence and metastasis in granulosa-cell tumors were nearly always confined to older patients. In only 1 other case[10] was there a definitely malignant metastasizing tumor; unfortunately, no photomicrographs were included. In another instance, the neoplasm was adherent to surrounding viscera[7]; the patient concerned was living and well 5½ years after treatment.

The fact that the neoplasm in our case was recurrent and associated with pregnancy is most unusual. As already mentioned, we could find no other such case report. It appears reasonable to assume that the neoplasm in this case had been present from the start of pregnancy, at which time it probably was not functioning to any significant degree. Whether or not it was responsible for the gushing vaginal bleeding cannot be stated.

Although this neoplasm was large and recurrent, the patient has had a satisfactory course for 10 months after operation and roentgen therapy. It is difficult to evaluate the effect of radiation treatment in these tumors but such treatment occasionally does appear to be of definite benefit. One of us (Dockerty) and MacCarty[19] previously reported a 31 month arrest of a recurrent granulosa-cell tumor after a dose of only 1,200 mg. hr. of radium.

TABLE I. ACCEPTABLE* AND QUESTIONABLY ACCEPTABLE† CASES OF GRANULOSA-CELL TUMOR ASSOCIATED WITH PREGNANCY

CASE	AUTHOR, YEAR	AGE	GRA-VID-ITY	RACE	APPEARANCE		STATUS OF PREGNANCY	TREATMENT	FOLLOW-UP	ENDO-CRINE EFFECTS	COMMENT
					GROSS	MICROSCOPIC PATTERN					
1	Slamova, 1937	23	i	White	Left; 20 by 12 by 9 cm.; twisted stalk	Trabecular with occasional acini	5 months	Left adnexectomy	None	None	Presenting complaint, anorexia
2	Mitra, 1940	16	i	Bengali Hindu	Right; 2 pounds	Cylindroid	4 to 5 months; miscarriage 1 month postoperatively	Oophorectomy	Well; had healthy child 1 year postoperatively	None	Presenting complaint, pain and abdominal swelling
3	Powell and Black, 1940	30	viii	White	Left; 10 by 7 by 5 cm.; in broad ligament	Sarcomatous	5 months; miscarriage, then discovery of tumor	Local removal 4 months post partum	Well 10 months postoperatively; subsequent delivery at term	Repeated abortions	Presenting complaint, a mass
4	Henderson, 1942	37	ii	White	Microscopic in size	Follicular and cylindroid	Not stated; tumor found at therapeutic abortion	Oophorectomy	Well 10 months postoperatively	None	—
5	Bolli, 1947	24	i	White	Right; 20 by 16 by 16 cm.	Varied but more folliculoid	At 7 to 8 months delivered 2,200 gram viable girl	None; died of intraperitoneal hemorrhage due to rupture of tumor	Died immediately post partum	None	—
6	Diddle and O'Connor, 1951	22	i	–	Right; 10 by 8 by 5 cm.	Sarcomatoid	Term; delivered 3,400 gram girl; then tumor discovered	Right salpingo-oophorectomy 4 months post partum	4 years; no recurrence	None until after discovery of tumor	Tumor discovered 9 days post partum
7	Tweeddale and associates, 1955	37	i	White	Right; metastatic nodules	Sarcomatoid, malignant	3 months; 10 cm. fetus	Surgical and x-rays	Well 10 months postoperatively	Bleeding	—

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8	Spencer and Hollenbeck, 1947	40	viii	Negro	Right; 22 by 17 by 11 cm.	Granulosa-cell tumor	At 7 months delivered 1,600 gram baby	Surgical and 4,000 r x-rays	Well 5½ years	Menstrual change	Tumor attached to liver, transverse colon, and right iliac fossa
9	Greenhill, 1947	—	—	–	Right; "about 30 cm."	Granulosa-cell tumor	Apparently term; tumor discovered post partum	Right oophorectomy and one-half of left ovary	Alive 17 years postoperatively	None	Carcinoma of endometrium at age 57
10	Haines and Jackson, 1950	29	—	–	Tumor 0.6 cm. in diameter in wall of serous cyst	Strongly luteinized granulosa cells	39 weeks; cesarean section with removal of tumor; viable 3,200 gram boy	Left oophorectomy and partial salpingectomy	None	None	—
11	Greene, Smith and McClelland, 1950	27	Parous	White	Multiple nodules. On left, 10 by 8 by 7 cm.; nodule on right, 8 cm.	Malignant granulosa-cell tumor	4 months; 16 cm. fetus	Partial removal	Died 18 days postoperatively	Breasts tender; diagnosed preoperatively	Widespread metastasis

*Cases 1 through 7 are acceptable.
†Cases 8 through 11 are questionably acceptable.

Summary

This report presents the sixteenth case of granulosa-cell tumor associated with pregnancy described in medical literature. The patient, a 37-year-old woman, was studied and treated at the Mayo Clinic. The tumor in this case is of interest because, in addition to being associated with pregnancy, it also was recurrent and malignant; this is the first such case to be reported. Roentgen therapy appears to be of some value in the treatment of these tumors.

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LEUKEMIA AND PREGNANCY

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LEUKEMIA, claiming over 6,000 lives a year in the United States alone, has more than doubled its death rate in the last twenty-five years.[14] In viewing these statistics, however, we must realize that progress in clinical and laboratory methods leading to more complete and accurate diagnoses plays an important part in the detection of a rising death rate from leukemia. The physician may occasionally have the responsibility of dealing with a pregnancy in the woman with leukemia.

This paper is presented (1) to report 7 cases of leukemia and one case of lymphosarcoma and pregnancy, and (2) to attempt to correlate some of the impressions and conclusions in the literature concerning leukemia and pregnancy.

Materials and Methods

The records of the Hematology Clinic and the Department of Pathology were reviewed. During the past twenty-three years in the Hematology Clinic, 1,644 cases of leukemia were seen. From 1937 to April, 1954, there were 17,496 autopsies completed, which included 394 cases of leukemia. In all of this material, 7 cases of leukemia and one case of lymphosarcoma and pregnancy were found.

Case Reports

CASE 1.—M. A., No. 456291, a 34-year-old white woman, was first seen by us in October, 1945. Eighteen months before, she began to notice shortness of breath, weakness, palpitation, and was treated for anemia. Recently she had begun to develop petechiae and to bruise easily. On admission she exhibited gingival hyperplasia, generalized palpable adenopathy, and petechiae over the inner aspects of both legs. The liver and spleen were not palpable.

Laboratory.—There were 3.31 million erythrocytes, the hemoglobin was 9.8 Gm. per 100 c.c., the leukocyte count was 3,350 with a differential of polymorphonuclear leukocytes 4 per cent, small lymphocytes 34 per cent, intermediate lymphocytes 8 per cent, monocytes 26 per cent, monoblasts 28 per cent. A platelet count of 162,400, reticulocytes 2 per cent, hematocrit 37 per cent, and a corrected sedimentation rate of 1.1 mm. per minute were noted. Sternal bone marrow puncture revealed one toxic red blood cell, no megakarocytes, no clasmatocytes, and rare red blood cells. A "pure culture" predominately of monoblasts with a few monocytes was seen. The WBC:RBC ratio was 1:0.2.

Diagnosis.—Acute monocytic leukemia.

Course.—Because of the low platelet count, radiation therapy was contraindicated. Since the monocytic strain is stimulated by certain lipids, the recommended therapy was a low-fat diet, the use of ground pancreas as a source of lipocaic to aid in the proper utilization of fats, and transfusions as deemed necessary. The patient was again hospitalized in December, 1945, complaining of dyspnea and weakness. Physical examination

was essentially unchanged other than that the uterine fundus was the size of a four months' gestation. The patient, a primigravida, had previously had regular menstrual periods every 21 days necessitating 18 pads per period until the present four months of amenorrhea. A blood count showed RBC 2.2 million, hemoglobin 5.9 Gm. per 100 c.c., platelets 44,400, reticulocytes 1.2 per cent, WBC 5,350 with a differential of active polymorphonuclear leukocytes 5 per cent, myelocytes "C" 1 per cent, small lymphocytes 27 per cent, intermediate 4 per cent, large 1 per cent, active monocytes 24 per cent, monoblasts 37 per cent, polymorphonuclear eosinophils 1 per cent. During the next two months of hospitalization, the patient received 30 whole blood transfusions. On Feb. 8, 1946, her temperature rose to 102.4° F. and she complained of marked pain on the right side. A diagnosis of obstruction of the right ureter with resulting renal infection was confirmed, and a ureteral catheter was passed, relieving the obstruction. The patient, in spite of heavy therapy, continued to have spiking temperatures and in this very precarious state went spontaneously into labor and delivered a stillborn male infant on Feb. 12, 1946. No unusual bleeding occurred at delivery or post partum. The patient became oliguric, the blood urea nitrogen rising to 56.5 mg. per 100 ml. of blood, and she died 57 hours post partum.

Autopsy.—The final diagnoses were: (1) monocytic leukemia with leukemic infiltration of bone marrow, heart, lungs, spleen, kidneys, and agranulocytosis; (2) bilateral pleural effusion; (3) pericardial effusion; (4) congestion and edema of the heart; (5) pulmonary atelectasis, congestion, interstitial hemorrhage and edema; organized infarct; (6) fatty infiltration of the liver; (7) lipoid depletion of the adrenal glands; cortical adenoma.

Autopsy of the Infant.—The premature male infant weighed 1,100 grams, with findings of subarachnoid and intraventricular hemorrhage of the brain, congestion of the brain, pulmonary atelectasis, subepicardial and periaortic petechiae, hemorrhagic necrosis of the adrenal glands, congestion and interstitial hemorrhage of the thymus gland. No evidence of a leukemic process was seen.

Comment.—This is a case of acute monocytic leukemia and pregnancy. Death occurred approximately five months after the patient first noticed petechiae and ecchymoses, and fifty-seven hours post partum. The patient was critically ill before the onset of labor.

CASE 2.—B. W., No. 491953A, a 28-year-old white woman, first noticed the onset of fatigue, shortness of breath, and some vertigo with nausea when she was two months pregnant. This was followed by a progressive pallor and gingival hyperplasia. When she was referred to us she was five months pregnant with a previous obstetrical history of two normal full-term deliveries, the first being associated with a vaginal hemorrhage two weeks post partum and necessitating a blood transfusion. Physically she was a pale white woman without evidence of petechiae or ecchymotic areas. There was a recent hemorrhage in the fundus of the right eye. The gingivae were markedly hyperplastic. There were palpable cervical nodes. The liver and spleen were not palpable, and the uterine fundus was at the umbilicus.

Laboratory.—The blood count showed RBC 1.79 million, hemoglobin 6.3 Gm. per 100 c.c., WBC 2,600 with polymorphonuclear neutrophils 56 per cent, polymorphonuclear eosinophils 4 per cent, small lymphocytes 20 per cent, monocytes 18 per cent, and monoblasts 2 per cent. The monoblasts seen in the peripheral blood contained Auer bodies. Reticulocytes 2.8 per cent, platelets 900,000, a normal fragility test, and a corrected sedimentation rate of 0.4 mm. per minute were found. A sternal bone marrow puncture disclosed an occasional blast cell with Auer bodies.

Diagnosis.—Acute monocytic leukemia.

Course.—Supportive therapy, consisting of blood transfusions as indicated until delivery, was decided upon. The patient subsequently received 30 whole blood transfusions until July, 1949, when she was delivered uneventfully of a full-term normal healthy female infant. Microscopic examination of the cord and placenta showed no abnormalities. A postpartum bone marrow specimen was obtained and showed only slight infiltration of

monoblasts with an occasional Auer body seen. As had been previously noted there was little erythropoiesis and the WBC:RBC ratio was 1:0.035. The postpartum peripheral blood count showed RBC 4.35 million, hemoglobin 12.5 Gm. per 100 c.c., WBC 28,000 with polymorphonuclear leukocytes 80 per cent, lymphocytes 7 per cent, myelocytes 1 per cent, active monocytes 7 per cent, young monocytes 1 per cent, monoblasts 4 per cent, reticulocytes 0.2 per cent, and platelets 140,480. Her postpartum course per se was uneventful. The marked hypertrophy of the gingivae continued, and the blood picture deteriorated. In spite of supportive therapy, the patient continued to grow worse and on Sept. 18, 1949, she died in her home town. No autopsy was obtained.

Comment.—This is another case of acute monocytic leukemia and pregnancy. Death occurred about nine months after the onset of symptoms and two months, eighteen days post partum.

CASE 3.—K. S., No. 422337, a 24-year-old white woman, received three x-ray treatments over the ovaries and pituitary gland in March, 1941, for what was described as menstrual irregularities and dysmenorrhea. Her first pregnancy began in May, 1941, and the patient did well until she was about five months pregnant when she first noticed painless swelling of the left side of the neck and shoulder, pronounced fatigue, weakness, and shortness of breath. Two weeks before term she was first noted to have anemia and received three blood transfusions. There had been no bleeding noted in the prenatal course. She delivered a full-term female infant uneventfully and during her postpartum hospitalization she received four more transfusions to correct the anemia. This patient was first seen by us in April, 1942, six weeks post partum, complaining of weakness and scanty vaginal bleeding. Physically, she was a very pale white woman who had generalized discrete, nontender, palpable adenopathy. The spleen was palpable just below the left costal margin.

Laboratory.—A blood count showed RBC 1.78 million, hemoglobin 7.2 Gm. per 100 c.c., WBC 2,800 with a differential of polymorphonuclear neutrophils 20 per cent, polymorphonuclear eosinophils 2 per cent, small lymphocytes 48 per cent, intermediate 10 per cent, lymphosarcoma cells 16 per cent, monocytes 2 per cent, young monocytes 2 per cent, reticulocytes 0.4 per cent, platelets 136,000, anisocytosis 4 plus, poikilocytosis 2 plus. A bleeding time of 6 minutes and coagulation time of 5 minutes were noted. The bone marrow showed 2.5 per cent myelocytes "C," 0.5 per cent myelocytes "A," 1.0 per cent polymorphonuclear eosinophilic myelocytes "C," and 96 per cent lymphosarcoma cells. The red blood count in a field of 200 WBC showed 8 normoblasts, 1 late erythroblast, and the WBC:RBC ratio was 10:1 with the lymphosarcoma cells predominating.

Diagnosis.—Acute lympholeukosarcoma (acute lymphatic leukemia), subleukemic or aleukemic phase.

Course.—The patient was treated with repeated small doses of x-ray to the spleen totaling 350 r. She returned to her home where she was given 100 r to the spleen one month later and also was given supportive blood transfusions. In spite of the therapy the patient continued to grow progressively worse and died in August, 1942, in her home town. No autopsy was obtained.

Comment.—This is a case of acute lymphatic leukemia and pregnancy. The patient died nine months after the onset of her symptoms and five months post partum. The newborn infant's blood count was normal and when she was 5 years old it was still perfectly normal.

CASE 4.—B. S., No. 467868, a 21-year-old white girl, was first seen here in November, 1946, with a two months' history of progressive weakness, easy fatigability, and enlarging abdomen. The menstrual history was normal. Physical examination showed pale mucous membranes, a massively enlarged spleen which filled the pelvis, and the liver was palpated 2 cm. below the right costal margin.

Laboratory.—A blood count showed 2.0 million RBC, hemoglobin 6.2 Gm. per 100 c.c., platelets 260,000, reticulocytes 9.4 per cent, WBC 669,000 with a differential of polymorphonuclear neutrophils 15 per cent, polymorphonuclear basophils 2 per cent, poly-

morphonuclear eosinophils 10 per cent, myelocytes "A" 2 per cent, myelocytes "B" 9 per cent, myelocytes "C' 6 per cent, and myeloblasts 2 per cent. A sternal bone marrow puncture showed the marrow to be very cellular. There were only moderate amounts of fat present. Hyperplasia of the granulocytes mainly at the "C" and polymorphonuclear levels and many megakarocytes were seen. Also an occasional myeloblast was noted. The WBC:RBC ratio was 1:0.035.

Diagnosis.—Chronic myelogenous leukemia.

Course.—The patient was given blood transfusions and 13 x-ray treatments to the spleen. After twenty days of hospitalization the WBC was 34,000, and she was discharged to be followed as an outpatient, being treated with radioactive phosphorus (P^{32}). Hospitalization occurred again in January, 1947, because of vaginal bleeding of seven weeks' duration. At this time the spleen was 4 cm. below the left costal margin and the WBC was 1,050, RBC 2.94 million, hemoglobin 7.8 Gm. per 100 c.c., and platelets 35,280. She was given transfusions and treatment with P^{32} continued. In July, 1948, she was started on Urethane. Her last normal menstrual period was Sept. 26, 1948, and this was followed by marked nausea and vomiting in November. The Friedman test was positive and in December a therapeutic abortion was carried out, the histopathological report showing chorionic villi with some hydropic degeneration. Postoperatively the patient did well and was followed as an outpatient until March, 1951, when she was hospitalized because of increasing fatigue, and some fever with weakness. The blood count on admission showed RBC 3.5 million, hemoglobin 9.5 Gm. per 100 c.c., WBC 12,500 with a differential of polymorphonuclear neutrophils 4 per cent, polymorphonuclear basophils 38 per cent, lymphocytes 26 per cent, myelocytes "A" 16 per cent, myelocytes "B" 4 per cent, myeloblasts 12 per cent, and no platelets or reticulocytes. Throughout her twenty-one days of terminal hospitalization the WBC dropped to levels as low as 66 and the RBC to 1.9 million. At no time were platelets or reticulocytes seen suggesting normal bone marrow activity. During this twenty-one days' stay the patient received 1,050 r to the spleen, and 2,500 c.c. of blood plus other supportive therapy. She maintained a febrile course, developed a hemorrhagic diathesis from all orifices of the body, and died on the twenty-first hospital day.

Autopsy.—The findings were: (1) chronic myelogenous leukemia with (a) myelophthisic anemia, (b) infiltration of the spleen, liver, lymph nodes, and bone marrow, and (c) purpura and petechiae of the skin, mucous membranes, mediastinum, renal pelves, and endometrium; (2) severe pulmonary edema and hemorrhage; (3) fungus inflammation of the stomach and colon with necrosis and ulceration.

Comment.—This case of chronic myelogenous leukemia was unusual in the fact that the patient became pregnant two years after the onset of the disease. She died four and one-half years after the onset of symptoms and two years, three months after a pregnancy which was therapeutically aborted at two months' gestation.

CASE 5.—J. G., No. 513853, a 40-year-old white woman, was first seen by us in July, 1951, with complaints of amenorrhea of four months' duration, weakness, night sweats, loss of appetite, a 10 pound weight loss bringing her weight down to 80 pounds, shortness of breath, and an enlarging abdomen. Physically she was an emaciated white woman with a markedly protuberant abdomen. There was generalized pallor of the skin and mucous membranes. No remarkable adenopathy was noted. The liver was palpable 5 cm. below the right costal margin. The spleen extended to the left iliac crest.

Laboratory Findings.—A blood count showed RBC 1.9 million, hemoglobin 6.3 Gm. per 100 c.c., platelets 145,160, reticulocytes 1.8 per cent, WBC 563,000 with a differential of polymorphonuclear neutrophils 37 per cent, polymorphonuclear basophils 2 per cent, polymorphonuclear eosinophils 2 per cent, myelocytes 56 per cent, myelocytes "A" 1 per cent, myeloblasts 2 per cent. A sternal bone marrow puncture showed it to be extremely hyperplastic for myeloid elements which were at the "C" level. There were infrequent megakaryocytes and markedly reduced erythropoiesis with no maturation arrest. There was an increase in basophilic granulocytes.

Diagnosis.—Chronic myelogenous leukemia.

Course.—The patient was treated with x-ray to the spleen, blood transfusions, and Urethane during her eight-day hospitalization and was then closely followed in the Hematology Clinic with varying dosages of Urethane as indicated by the clinical and laboratory findings. A three and one-half months' pregnancy was noted in July, 1952, on a routine visit to the clinic. Urethane therapy was discontinued for the remainder of the prenatal course which passed without complications. In December, 1952, the patient delivered her eighth child, a normal full-term healthy infant, without difficulty. Obstetrically, the postpartum course was entirely benign. Hematologically, the postpartum blood count showed RBC 4.04 million, hemoglobin 12.4 Gm. per 100 c.c., reticulocytes 2 per cent, platelets 2,424,000, WBC 66,000 with a differential of active polymorphonuclear neutrophils 52 per cent, polymorphonuclear basophils 1 per cent, polymorphonuclear eosinophils 1 per cent, myelocytes "C" 45 per cent, myelocytes "A" 1 per cent. The spleen was below the left iliac crest, the liver 10 cm. below the right costal margin on her third postpartum day. The patient was started on radioactive phosphorus (P^{32}) and has since received dosages in the hematology follow-up as indicated by the clinical and laboratory findings. On her most recent visit to the clinic in April, 1954, her WBC was 39,000, and she was given 2 mc. of P^{32}.

Comment.—This is a case of chronic myelogenous leukemia in a 41-year-old white woman who conceived and carried a pregnancy to term without difficulty. The leukemia is now of about three years' duration, and the patient sixteen months post partum and doing well.

CASE 6.—F. D., a 32-year-old white women, had an essentially uneventful prenatal course and delivered her second full-term healthy infant without difficulty in July, 1953. On the third postpartum day a routine blood count disclosed an alarmingly high white count. She was first seen here in August, 1953, her only complaint being some pain in the right leg. Physically she was markedly overweight. There was no demonstrable adenopathy, petechiae, purpura, or hepatomegaly. The spleen was palpated 2 cm. below the left costal margin on deep inspiration.

Laboratory.—A blood count showed RBC 4.1 million, hemoglobin 11.3 Gm. per 100 c.c., platelets 697,000, reticulocytes 3.8 per cent, WBC 178,000 with a differential of polymorphonuclear leukocytes 35 per cent, myelocytes "C" 59 per cent, myelocytes "B" 2 per cent, lymphocytes 2 per cent, and monocytes 2 per cent. The hematocrit was 36 per cent, the sedimentation rate 51 mm. in 60 minutes. Sternal marrow studies showed it to be markedly hyperplastic for myeloid cells at the late myelocyte and polymorphonuclear level. Only an occasional myeloblast was found. Normoblasts were quite frequent. The megakaryocytes were present in at least normal numbers.

Diagnosis.—Chronic myelogenous leukemia.

Course.—The patient was given 4.5 mc. of P^{32} and was seen again in six weeks. At this time there was a satisfactory response to the P^{32} with the blood count findings of RBC 3.75 million, hemoglobin 11.7 Gm. per 100 c.c., platelets 817,500, reticulocytes 6.8 per cent, WBC 71,000 with the differential of polymorphonuclear leukocytes 68 per cent, myelocytes "C" 20 per cent, lymphocytes 4 per cent, and monocytes 8 per cent. She was given an additional 3 mc. of P^{32} and since has been followed with blood counts noting the response of the radioactive material. The white count has remained below 30,000 and the differential essentially unchanged. The RBC and hemoglobin have remained fairly stable. A letter from her private physician noted the fact as of the middle of April, 1954, the patient was again about three months pregnant.

Comment.—This patient with chronic myelogenous leukemia is now about ten months post partum from the birth of her second child, is now about three months pregnant for the third time, and thus far appears to be doing well.

CASE 7.—S. A., a 31-year-old white woman, had a unique prenatal course in the fact she had a weight loss from a usual 134 to 115 pounds. During the last trimester she noticed an occasional scanty episode of epistaxis. She delivered a normal full-term infant on

August 16, 1952, and at that time the spleen was found to be enlarged down to the umbilicus. A reported blood count was hemoglobin 14.0 Gm. per 100 c.c., WBC 342,000 with a differential of 42 per cent neutrophils, 20 juveniles, 12 myelocytes, 3 lymphocytes, 1 eosinophil, and 22 band forms. She was treated with 450 r to the splenic area, started on Urethane, and within a few weeks was showing a good response to the treatment. Her first postpartum menstrual period occurred on Oct. 28, 1952. The patient was first seen by us in December, 1952. Physically she appeared in good health, skin and mucous membranes showing good color. The liver and spleen were not palpable and there was no generalized adenopathy.

Laboratory.—A blood count showed RBC 4.93 million, hemoglobin 14.1 Gm. per 100 c.c., platelets 414,120, reticulocytes 1 per cent, WBC 5,950 with the differential of actively motile neutrophils 83 per cent, basophils 2 per cent, eosinophils 1 per cent, myelocytes "C" 3 per cent, myeloblasts 2 per cent, lymphocytes normal small mature 4 per cent, mature normal active monocytes 5 per cent. The hematocrit was 45 per cent, and the corrected sedimentation rate was 0.8 mm. per second.

Diagnosis.—Chronic myelogenous leukemia.

Course.—It appeared that this patient had shown an optimum response to the previously administered therapy. It was suggested that if remission in the hematologic picture should occur, reinstitution of Urethane should be carried out or if radioactive phosphorus were available it should be used. Deep x-ray therapy over the spleen was recommended if splenomegaly should occur. The patient returned to her home where her physician maintained her in Urethane and blood transfusions. She did well until July, 1953, at which time an exacerbation of the disease process occurred with a WBC of 195,000 reported. Additional x-ray therapy to the spleen was utilized with a good response, but another exacerbation occurred in September, 1953, with the WBC being 168,000 with a differential of 92 per cent myeloblasts, 2 per cent myelocytes, and 6 per cent polymorphonuclear neutrophils. The RBC was 2.5 million, hemoglobin 8.0 Gm. per 100 c.c., platelets 50,000, with a normal prothrombin and clot retraction. The spleen filled most of the abdomen at this time. A bone marrow study found marked myeloid hyperplasia with a marked depression of the erythroid elements. She was treated with x-ray to the spleen, multiple blood transfusions, Urethane, and cortisone, but progressive deterioration continued and she died on Oct. 11, 1953.

Autopsy.—The postmortem conclusions were: (1) acute exacerbation of chronic myelogenous leukemia; (2) leukemic infiltration of heart, liver, spleen, uterus, and ovary; (3) splenomegaly; (4) hepatomegaly; (5) infarctions of spleen and ovary; (6) multiple cerebral and cerebellar hemorrhages; (7) epicardial and subendocardial hemorrhages; (8) pericardial effusion; (9) peripheral atelectasis, minimal, lower lobe, bilateral; (10) parathyroid cyst.

Comment.—This is a case of chronic myelogenous leukemia which was diagnosed in the immediate postpartum period. The patient died fourteen months after the diagnosis was made during her postpartum hospitalization. The infant is alive, doing well, and has no evidence of a leukemic process.

CASE 8.—D. H., No. 502064A, a 26-year-old white woman, noticed progressive weakness in January, 1948, eight months following the delivery of her first child, and a blood count showed her to be anemic. When she was seen here, physical examination showed a patient with a slight pallor and generalized adenopathy. The spleen was massively enlarged, the liver slightly enlarged, and both organs were tender to palpation.

Laboratory.—A peripheral blood count showed RBC 4.23 million, hemoglobin 11 Gm. per 100 c.c., platelets 304,560, reticulocytes 1.4 per cent, WBC 4,550 with a differential of neutrophils 47 per cent, lymphocytes 46 per cent, and monocytes 7 per cent. Many of the lymphocytes in the peripheral blood were immature with scanty cytoplasm and prominent nucleoli. A few of these showed highly refractile bodies within the cytoplasm and were highly suspicious of lymphosarcoma. A sternal bone marrow study showed a very hyperplastic tissue with myeloid and erythroid elements in abundance. Megakarocytes

were also plentiful and appeared relatively normal. There was a slight shift to the late erythroblastic level. The marrow tissue, however, showed invasion of many lymphocytes which were characteristic of lymphosarcoma cells similar to those seen in the blood stream.

Diagnosis.—Lymphosarcoma.

Course.—The patient was treated with x-ray to the spleen and also started on P^{32} and followed as an outpatient with the dosage of P^{32} varying with the clinical and hematological picture. She became pregnant in August, 1949, and did well until the eighth month at which time a hemolytic episode occurred with the spleen palpable 3 cm. below the left costal margin, anemia, and reticulocytes 17 per cent. Studies of survival of red blood cells, fragility, and bone marrow confirmed the diagnosis of an acquired hemolytic anemia. The patient later delivered uneventfully a full-term healthy infant. No abnormality of the cord or placenta was noted. During the puerperium the hemolytic episode became quiescent and the spleen was no longer palpable. She was followed as an outpatient with dosages of P^{32} as indicated by the clinical and hematological pictures. In October, 1952, she was complaining of chronic fatigue and stated she believed she was pregnant. Examination showed the size of the uterus to be compatible with a two months' gestation. One month previously the patient had received 2 mc. of P^{32}. During the next three months the spleen enlarged considerably. In December, 1952, at which time she was five months pregnant, a splenectomy was performed, the spleen weighing 1,600 grams. A liver biopsy showed neoplastic infiltration. There were numerous large retroperitoneal nodes palpated at the laparotomy. She uneventfully delivered a full-term healthy infant in May, 1953, and at that time there were excellent blood pictures in both the mother and the infant. Since then the patient has been receiving P^{32} and also x-ray treatments to markedly enlarging cervical nodes. At the present time this patient is again pregnant and so far has refused to seek prenatal care.

Comment.—This is a case of lymphosarcoma and pregnancy. Erf[5] in his report gave only two references to previous cases of lymphosarcoma and pregnancy. This case is unusual in the fact that the patient is now pregnant for the third time during the course of her disease; also that a splenectomy was performed during one of her pregnancies. McElin and co-workers[12] reported 5 cases of splenectomy during pregnancy, reviewed the literature, and noted no untoward results of splenectomy in pregnancy, thereby agreeing with an earlier report by Barnes and Doan.[3]

Comment

Pregnancy is a rare occurrence in the woman with leukemia. Review of the literature of leukemia and pregnancy by several authors[5, 6, 7, 13, 18] has been carried out. The recent review by Harris[8] of 114 cases included 3 cases of acute monocytic, 12 of acute lymphatic, 27 of acute myelogenous, 3 of chronic lymphatic, and 69 of chronic myelogenous leukemia and pregnancy.

In the past twenty-three years at the Hematology Clinic of the Ohio State University Health Center, 1,644 cases of leukemia have been seen and only 7 of these were associated with pregnancy. What could be the reasons for such a paucity of pregnancies in leukemic women? Some of the general considerations which would make the simultaneous occurrence of leukemia and pregnancy understandably rare are the infrequency of pregnancies with debilitating diseases, the usual short life course in acute leukemia, and the fact that chronic leukemia is more commonly seen in the older age group. Further factors limiting the number of cases actually reported include the initiation of contraceptive techniques when the diagnosis and prognosis of the disease are learned by the affected individuals, infertility in either partner, and cases of leukemia and pregnancy which have never been reported.

More specifically leukemic infiltration of the female organs with secondary amenorrhea has been considered to be a factor.[1, 9, 11, 13, 15, 17] In a review of the records of 17,496 autopsies completed from 1937 to April, 1954, by the Department of Pathology, there were 394 autopsied cases of leukemia, 245 (62.2 per cent) males and 149 (37.8 per cent) females. Of 105 females whose histopathological report included any or all of the reproductive organs, 40 (38.1 per cent) showed leukemic infiltration of uterus and/or tube and/or ovary. It can be postulated that this incidence would be much higher if multiple sections and very careful microscopic examination of the reproductive organs had been carried out.

To evaluate menstrual irregularities, examination of the hospital charts of 43 autopsied women with leukemia whose disease process occurred between the menarche and the menopause was done. Nineteen showed leukemic infiltration of the female organs, and of these 19 patients, 8 had no menstrual irregularities, 2 had amenorrhea, and 9 had menorrhagia occurring before the diagnosis of leukemia was made. Conversely, in 24 patients no leukemic infiltration of the reproductive organs was noted, and 5 had menorrhagia, 3 had amenorrhea, and 16 had regular menses. One-third (14) of these patients had histories of menorrhagia. With the hemorrhagic tendencies frequently seen in leukemia, this menorrhagia is not surprising. Barnes[2] has suggested a possible mechanism for the hypermenorrhea seen in patients with hematologic bleeding tendencies. He presented the ideas that "(1) a woman with hemorrhagic blood dyscrasia will not acquire hypermenorrhea without the intermediary of a local pelvic abnormality; (2) from the strictly gynecologic point of view this local finding would usually be considered sufficient to explain the bleeding organically, or to justify the diagnosis of functional bleeding of presumed endocrine cause; and (3) in most instances the local pelvic lesion itself results from the coagulation defect of the circulating blood (tubal hemorrhages, chocolate cysts of the ovary, etc.)."

Hemorrhages following vaginal or operative deliveries are uncommon when one notes the extent to which the patient's blood picture may be altered by the leukemic process. Harris[8] noted only three fatal hemorrhages as reported in 1929, 1931, and 1950, in 114 cases of leukemia and pregnancy.

There have been conflicting reports in the literature as to whether pregnancy in leukemic patients exerts any influence on their longevity. A review of the histories of 149 autopsied women, noting the time interval from the onset of symptoms which prompted the patient to seek medical attention, until death occurred, showed an average span of 3.82 months in the acute leukemias and of 28.44 months in the chronic leukemias. Both of these results would probably be much higher if only the recently diagnosed cases were under consideration since during the past few years the introduction of new drugs and techniques has raised the life expectancy in both the acute and chronic leukemias much higher than reported here. In the 7 cases of leukemia with pregnancy, this time interval was 7.67 months in the three acute cases and 28.5 months plus (two patients are still alive and doing well) in the

chronic cases seen in pregnancy. From a comparison of these figures, it appears that pregnancy does not shorten the life expectancy of a pregnant as compared to a nonpregnant leukemic patient. While Wiseman[20] believes that pregnancy does not influence the longevity of the leukemic woman, the question of whether pregnancy may actually lengthen the life span in leukemia is not settled from the present study. In this respect it is of interest to note again the length of survival from the onset of symptoms in the pregnant versus the nonpregnant leukemic patient. In the pregnant patients with leukemia, the average survival of 7.67 months in the acute and 28.5 months (with two patients still alive) in the chronic leukemias appears favorable as compared to the 3.82 months and 28.44 months, respectively, in the nonpregnant acute and chronic cases. Although these figures might indicate a trend, a much larger number of cases would have to be studied in order to demonstrate the favorable effect—if any—of pregnancy upon the course of leukemia.

True exacerbations of the leukemia did not occur during the pregnancies in the cases reported here. Many authors[7, 9, 13, 15, 18, 19] believe, therefore, that pregnant patients with leukemia should not have therapeutic abortions, but should be allowed to carry the pregnancy to term if possible. Our results seem to substantiate this fact. Consequently, such patients should be allowed to go to term if possible with vaginal delivery contemplated, and cesarean section should be reserved only for the usual obstetric indications or else in an attempt to save an infant of a moribund mother.

It appears that the placenta acts as a barrier to leukemia since no mother with leukemia has been reported to give birth to a leukemic child.[18] There have been cases of congenital leukemia reported,[4, 10, 16] but in all cases the mother had shown no evidence of the disease.

Many different types of treatment have been employed in the leukemic patient such as x-ray, radioactive phopshorus, Urethane, Aminopterin, Fowler's solution (potassium arsenite), nitrogen mustard, and triethylene melamine (TEM), with improvement of the patient's condition, but there is still no known cure for leukemia.

Conclusions

1. Seven cases of leukemia and one case of lymphosarcoma and pregnancy have been reported representing the largest single series reported from a single institution.

2. There was no exacerbation of the leukemic process during pregnancy in these patients and no evidence of leukemia was noted in the offspring.

3. The possibility that pregnancy may favorably affect the course of leukemia in certain cases has been considered.

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THE CHANGING ASPECTS OF PNEUMONIA COMPLICATING PREGNANCY

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WHILE pneumonia as a deadly complication of pregnancy is almost a thing of the past, students of the history of medicine may find this review of interest. Hippocrates stated his opinion that acute diseases occurring during pregnancy are dangerous, and often terminate fatally. In 1694 Mauriceau recorded the case of a woman, in the sixth month of pregnancy, who aborted on the ninth day of her pneumonia, and died on the thirteenth. Although pneumonia is no longer the perilous complication of pregnancy that it once was, the statistics of the New York Lying-In Hospital for the years 1932 to 1943 showed that pneumonia accounted for 7.5 per cent of all maternal deaths, being surpassed only by hemorrhage and puerperal infection.

The preparation of this report includes a review of the literature and an analysis of the records of the Royal Victoria Hospital from 1926, when the Women's Pavilion was opened, to the end of 1953.

Incidence.—

At one case of pneumonia per 1,000 pregnancies, the incidence of this condition is low (Table I). In 1905 Ransdell reviewed the German, French, Italian, and English literature for the previous 200 years. He collected 350 cases, and added 2 of his own. In the Royal Victoria Hospital series there were 100 cases of pneumonia associated with pregnancy. Thirty-six of these occurred post partum, while 64 were ante partum, and it is with the latter that this report is mainly concerned.

TABLE I. INCIDENCE OF PNEUMONIA DURING PREGNANCY

	TOTAL PREGNANCIES	PNEUMONIA	PERCENTAGE
Oppel	15,000	15	0.10
Royal Victoria Hospital	60,000	64	0.11
Nuckels	20,364	23	0.12
Schmitt	35,000	44	0.13

Interruption of Pregnancy.—

The mechanical interference with lung expansion in pregnancy, especially during the later months, greatly adds to the dyspnea of the patient with pneumonia. The consolidation of a portion of one or both lungs interferes with the normal oxygenation of mother and fetus. Interruption of the pregnancy occurs frequently (Table II).

In 40 (or 63 per cent) of the 64 patients in the Royal Victoria Hospital series the pregnancy came to an end during the course of the acute illness. In the first six months of gestation 17 per cent aborted, while in the third trimester, from the twenty-fifth to the thirty-sixth week, the figure for termination rose to 71 per cent. We have set apart the period from the thirty-seventh

to the fortieth week because these patients were near to term, and many might have gone into labor anyway. The incidence of delivery in this latter group was 90 per cent.

Cragin reported that pneumonia interrupted the pregnancy in 40 per cent of cases during the first half and 60 per cent during the second half of gestation. Ransdell found that of 144 patients with pneumonia in the first 6 months of gestation 52 per cent aborted, while of 164 in the last trimester delivery took place in 70 per cent. DeLee pointed out that pregnancy is interrupted spontaneously in about two-thirds of patients with pneumonia, and that the more advanced the pregnancy the more frequently is gestation terminated. Beck suggested that the tendency to abortion and premature labor is caused by profound toxemia, high temperature, and anoxemia. Finland noted that pregnancy came to an end in 55 per cent, and more often in the fatal cases than in those patients who recovered.

TABLE II. TERMINATION OF PREGNANCY IN RELATION TO PERIOD OF GESTATION

	NO. CASES	NO. DELIVERED	PERCENTAGE DELIVERED
First 24 weeks	18	3	17
25-36 weeks	24	17	71
37-40 weeks	22	20	90
Total	64	40	63

Antibiotics and Interruption of Pregnancy.—

Comparison of the incidence of interruption of pregnancy during pneumonia between those patients who did not and those who did have the benefit of the modern antimicrobial drugs disclosed that the beneficial effect of these drugs was not in this particular aspect. As shown in Table III, the incidence of termination of pregnancy in the important period of 25 to 36 weeks is not different before and after the introduction of the antibiotics. In the thirty-seventh to the fortieth week group, the number of pregnancies which came to an end was not strikingly reduced by the use of these drugs.

TABLE III. EFFECT OF ANTIMICROBIAL DRUGS ON INTERRUPTION OF PREGNANCY

	NO. CASES	NO. DELIVERED	PERCENTAGE DELIVERED
Before Antimicrobial Drugs.—			
First 24 weeks	9	2	22
25-36 weeks	10	7	70
37-40 weeks	16	15	93
Total	35	24	69
During Use of Antimicrobial Drugs.—			
First 24 weeks	9	1	11
25-36 weeks	14	10	71
37-40 weeks	6	5	83
Total	29	16	55

Antiobiotics and Maternal Mortality.—

The total mortality rates as given by Ricau in 1874 and Ransdell in 1905 are similar (Table IV). Ricau, with 12 deaths in 43 cases of pneumonia during pregnancy, noted a mortality rate of 28 per cent. Ransdell, with 96 deaths in 352 cases, reported a death rate of 27.3 per cent.

In our own series there was a total of 8 deaths in 64 cases to give a mortality rate of 12.5 per cent. When this figure is broken down we note a death rate of 20 per cent (or 7 deaths in 35 cases) before the use of the modern anti-

microbial drugs, and a marked drop to 3.5 per cent (or 1 death in 29 cases) during the antibiotic era. Thus the high death rate from pneumonia in pregnant women has been markedly reduced by the antimicrobial drugs.

TABLE IV. EFFECT OF ANTIBIOTICS ON MATERNAL MORTALITY

	NO. CASES	NO. DEATHS	PERCENTAGE
Series of Ransdell	352	96	27.3
Series of Ricau	43	12	28.0
Royal Victoria Hospital			
Entire series	64	8	12.5
Before antibiotics	35	7	20.0
With antibiotics	29	1	3.5

Maternal Mortality and Duration of Pregnancy.—

The mortality rate rises with the duration of the pregnancy (Table V). In our series this is shown by the figures of 5.5, 8.3, and 22.7 per cent for the first six months, the twenty-fifth to the thirty-sixth week, and the thirty-seventh to the fortieth week, respectively.

TABLE V. MATERNAL MORTALITY IN RELATION TO DURATION OF PREGNANCY

	NO. CASES	NO. DEATHS	PERCENTAGE
First 24 weeks	18	1	5.5
25-36 weeks	24	2	8.3
37-40 weeks	20	5	22.7
Undelivered	24	2	8.3
Delivered	40	6	15.0

Furthermore, a greater percentage of women who are delivered die than do those in whom the pregnancy goes on (Table V). Our finding of 15.0 per cent mortality in those who were delivered is almost double the 8.3 per cent of those who carried on. To put it differently, in 75 per cent of the patients who died the pregnancy had terminated.

Ransdell found that during the first six months of pregnancy 22 per cent of patients with pneumonia died, while in the last three months 30 per cent died. He pointed out that labor had an unfavorable effect on the maternal mortality as only 10.2 per cent of patients who did not go into labor died, while 36 per cent of those who were delivered died. Of the 96 patients who died, 85.4 per cent were in the group who were delivered. Finland found that 70 per cent of the deaths occurred in patients who were delivered.

Age and Maternal Mortality.—

Analysis of our findings from the standpoint of age disclosed that the lowest maternal mortality rate of 4 per cent was in women under 30 years of age (Table VI). In the 30 to 40 year age group the figure was 19 per cent, and in the group over 40 years of age the death rate was 16 per cent. Ransdell's figures are 13 per cent in the group under 25, 23 per cent in the 25 to 35 year group, and 22 per cent in women over 35 years of age.

Parity and Maternal Mortality.—

Ransdell found the death rate to be higher in primigravidas (31 per cent) than in multigravidas (25 per cent). Finland noted the opposite, namely, 37 per cent in multigravidas and 27 per cent in primigravidas. In our own series, the death rate in primigravidas was 18 per cent, compared to 10 per cent in multigravidas. If, however, from the multigravidas we separate the grand multigravidas (8 babies or more), we find the primigravidas with a mortality of 18 per cent, the ordinary multigravidas with 8 per cent, and the grand multigravidas at the top with 29 per cent (Table VI).

TABLE VI. MATERNAL MORTALITY IN RELATION TO AGE AND PARITY

	NO. CASES	NO. MATERNAL DEATHS	PERCENTAGE
Age.—			
Under 30 years	26	1	4
30-40 years	32	6	19
Over 40 years	6	1	16
Parity.—			
Primigravidas	17	3	18
Multigravidas with fewer than 8 babies	40	3	8
Multigravidas with 8 babies or more	7	2	29

Type of Pneumonia During Pregnancy.—

There was almost an equal number of cases of lobar and bronchopneumonia, 27 and 29 cases, respectively, and 8 atypical cases (Table VII). The maternal mortality was zero in the atypical group, 11 per cent in cases of bronchopneumonia, and rose to 19 per cent in lobar pneumonia. The highest fetal loss was in the cases of lobar pneumonia.

TABLE VII. TYPE OF PNEUMONIA DURING PREGNANCY IN RELATION TO MATERNAL DEATHS

	NO. CASES	NO. MATERNAL DEATHS	PERCENTAGE
Lobar	27	5	19
Broncho	29	3	11
Atypical	8	0	0

Postpartum Pneumonia.—

There were 36 cases of pneumonia after delivery (Table VIII). Three were of the atypical variety, 10 were lobar, and 23 were bronchopneumonia. In contrast to the antepartum period where the frequency of lobar and bronchopneumonia was about the same, the incidence of bronchopneumonia in the postpartum period was over twice that of lobar pneumonia. The mortality rate was zero for the atypical type, and 10 and 8.7 per cent, respectively, in the lobar and bronchopneumonia. The total postpartum mortality rate was 8 per cent. Before antibiotics the death rate was 25 per cent, or 3 out of 12. During the antibiotic age the mortality was zero (Table IX).

TABLE VIII. TYPE OF PNEUMONIA IN THE PUERPERIUM IN RELATION TO MATERNAL MORTALITY

	NO. CASES	NO. MATERNAL DEATHS	PERCENTAGE
Lobar	10	1	10.0
Broncho	23	2	8.7
Atypical	3	0	0

TABLE IX. EFFECT OF ANTIMICROBIAL DRUGS ON MATERNAL MORTALITY FROM PNEUMONIA IN THE PUERPERIUM

	NO. CASES	NO. MATERNAL DEATHS	PERCENTAGE
Before antimicrobial drugs	12	3	25
After antimicrobial drugs	24	0	0
Total	36	3	8

Fetal Mortality.—

The total fetal loss in our series was 22 per cent (Table X). If only those cases in which delivery took place are included the death rate was 35 per cent. To see any significance in these figures they must be broken down.

In cases where the pregnancy terminated we see the highest percentage of fetal loss (66 per cent) in the first six months. Next is the twenty-fifth to the thirty-sixth week group with 53 per cent. Lowest is the thirty-seventh to the fortieth week group with a fetal loss of only 15 per cent. The explanation is that, as term is approached and prematurity left behind, the chance for infant survival is increased.

TABLE X. FETAL LOSS FOR ENTIRE SERIES

	NO. CASES	NO. DELIVERED	NO. FETAL DEATHS	DEATHS AS A PERCENTAGE OF INFANTS DELIVERED	DEATHS AS A PERCENTAGE OF TOTAL CASES
First 24 weeks	18	3	2	66	11
25-36 weeks	24	17	9	53	38
37-40 weeks	22	20	3	15	14
Total	64	40	14	35	22

When both delivered and undelivered patients are included, we find that the smallest fetal loss (11 per cent) was in the first 24 weeks for the reason that the lowest incidence of termination of pregnancy lies in this period. The highest loss (38 per cent) was in the twenty-fifth to the thirty-sixth week. In this group we have a relatively high incidence of delivery plus the handicap of prematurity. Prematurity played a smaller role in the thirty-seventh to the fortieth week group where the fetal mortality was lower at 14 per cent even though the rate of delivery was higher.

Ransdell found that 41 per cent of infants born at a viable age died. Bullowa noted that of 25 babies born after the seventh month of gestation, 7 perished, a rate of 28 per cent. He ascribed the high fetal loss to prematurity, toxemia, anoxemia, and intrauterine infection. DeLee pointed out that pneumococci can pass through the placenta to the fetus, but that this occurs infrequently. In our series two babies died of pneumococcic infections of the same type as that of the mother, one with pneumonia, and one with pneumococcic meningitis.

Effect of Antibiotic Drugs on Fetal Loss.—

The striking effect of the antimicrobial drugs in reducing fetal loss is shown in Table XI. In the group from the twenty-fifth to the thirty-sixth week the fetal mortality, which was 71 per cent of the delivered cases and 50 per cent of the total cases, was reduced to 40 per cent and 29 per cent. In the thirty-seventh to the fortieth week group the fetal loss, which was 20 per cent of delivered and 19 per cent of total cases, was reduced to zero in those patients who had the benefit of the antibiotics.

TABLE XI. EFFECT OF ANTIBIOTICS ON FETAL LOSS

	NO. CASES	NO. DELIVERED	NO. FETAL DEATHS	DEATHS AS A PERCENTAGE OF INFANTS DELIVERED	DEATHS AS A PERCENTAGE OF TOTAL CASES
Before Antibiotics.—					
First 24 weeks	9	2	1	50	11
25-36 weeks	10	7	5	71	50
37-40 weeks	16	15	3	20	19
During Use of Antibiotics.—					
First 24 weeks	9	1	1	100	11
25-36 weeks	14	10	4	40	29
37-40 weeks	6	5	0	0	0

Treatment.—

As with many medical complications of pregnancy, treatment should be directed toward the pneumonia without active obstetrical interference. Certainly induction of labor is contraindicated. Beck urged that oxygen and morphine be given to prevent the onset of labor, and that pituitary extract, which was often used to relieve distention in patients with pneumonia, should be avoided in pregnancy. DeLee pointed out that the prognosis becomes worse when labor is induced, and warned against it. Bullowa stated that during the delivery there is a great demand for oxygen by both mother and fetus and advised that this be given in sufficient concentration to prevent cyanosis. In fact, the only obstetrical interference permissible is the performance of elective low forceps delivery to relieve the already embarrassed pulmonary and circulatory systems of the added strain of the bearing-down efforts. The anesthesia of choice is local infiltration.

Treatment is therefore medical and directed against the pneumonia. Review of our records shows that the advent of the antimicrobial drugs not only revolutionized the specific therapy of pneumonia, but brought about a change in the supportive treatment as well. The progress in specific treatment from nothing through the antisera to the antimocrobial drugs, running the gamut from the early sulfonamides to the antibiotics which are specifically concentrated in the lungs, is well known. The changes in supportive therapy are not so obvious (Table XII).

TABLE XII. INFLUENCE OF ANTIMICROBIAL DRUGS ON OTHER FORMS OF THERAPY

	BEFORE ANTIMICROBIAL DRUGS		AFTER ANTIMICROBIAL DRUGS	
	NO. CASES	PERCENTAGE	NO. CASES	PERCENTAGE
Total	47		53	
Oxygen	21	44.7	11	20.7
Expectorants	31	66	12	22.6
Stimulants	9	19.2	5	9.4
Digitalis	16	34.1	1	1.9
Poultices	26	55.4	7	13.2
Alcohol	25	53.3	0	0

Oxygen was used half as frequently in the antibiotic age as before it. However, the employment of oxygen might well be kept up even today as the antibiotics do not bring the pulmonary function back to normal as rapidly as they reduce the general toxic state. A normal temperature does not contraindicate the use of oxygen, which should be given to combat anoxemia in both mother and fetus.

The expectorants are used less often today as are the stimulants such as Coramine, Adrenalin, and caffeine. The use of digitalis to treat or prevent heart failure fell from 34 per cent in the earlier days to less than 2 per cent in the modern era. Linseed poultices or mustard plasters were placed on the chest and back in over 55 per cent of cases in the preantibiotic age, and in only 13 per cent in recent years. Regular small doses of brandy or whiskey which were almost routine are an almost forgotten remedy today.

Summary and Conclusions

We have presented a series of cases of pregnancy complicated by pneumonia in the Royal Victoria Hospital during the years 1926 to 1953, and a review of the literature.

Conclusions are:

1. Pneumonia was an infrequent but serious and often fatal complication of pregnancy.

2. In over half the cases the pregnancy terminated during the pneumonia, and more often in the late months of gestation. The antibiotic drugs did not reduce significantly the incidence of termination of pregnancy in our series.

3. The antimicrobial drugs have markedly reduced maternal mortality, both during pregnancy and in the puerperium.

4. The maternal mortality rate was higher in the latter part of pregnancy.

5. The death rate was higher in women who delivered than in those who did not.

6. The maternal mortality rate was lowest in the group under 30 years of age.

7. The highest maternal mortality rate was in the grand multigravida.

8. The incidence of lobar and bronchopneumonia was almost the same in the antepartum period, but in the postpartum group bronchopneumonia was twice as common.

9. In the puerperium the death rates from lobar and bronchopneumonia were about the same. During pregnancy lobar pneumonia was responsible for more maternal deaths than was bronchopneumonia.

10. Pneumonia in pregnancy resulted in a high fetal loss.

11. The use of the antibiotics has greatly reduced the fetal mortality.

12. The treatment is medical. Induction of labor is contraindicated.

13. The antibiotics have revolutionized treatment and prognosis.

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TRAUMATIC VULVAR HEMATOMAS

Report of Six Cases and Review of the Literature

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THE treatment of traumatic vulvar hematomas is mentioned scarcely or not at all in the standard textbooks on gynecology published in this country. In the literature, which is by no means voluminous, there seem to be differences of opinion regarding the treatment of traumatic hematomas of all sizes. No one person has had much experience with this condition. In this paper it will be our purpose to review the modern literature and extract pertinent therapeutic principles found therein. From this and our experience, we will attempt to outline a program of therapy which will be applicable to many traumatic nonpuerperal vulvar hematomas.

Historical

In the world literature this condition received the attention of European writers, predominately German, during the latter part of the last century and the early part of this century. Since then very few articles containing changes in therapy have appeared. As of 1911, 40 cases had been reported by German authors.[15, 35, 38] In this country, Steiner (1890),[44] Hirst (1896),[21] and Brickerer (1896)[5] reported one case each. Since then a search of the literature has failed to show further contributions by American authors.

Tables I and II list the cases we were able to find in the literature, including a group of cases collected since 1887 by Ohnaker.[35] These amount to a total of 54 cases up to July, 1954, not including the present group of 6 cases. Many of the data in earlier reported cases are incomplete so that all aspects could not be used. By way of contrast, puerperal hematomas have received more attention in the literature, especially in the last decade. Two hundred and sixty cases have been reported as of April, 1953.[31]

Only 8 cases of traumatic vulvar hematoma have been reported during the interval between 1920 and 1953 (Table II). This seems to be unusual in view of the fact that since 1920 women have enjoyed more freedom in all types of physical endeavor than at the turn of the century. While it is probably true that many cases have been seen during this period but not reported, on the basis of reported material, traumatic vulvar hematoma is an uncommon condition.

Anatomy and Pathology

The region of the female generative organs is very vascular, containing many small branches of the internal pudendal artery and vein, along with the highly vascular erectile tissue of the clitoris and vestibular bulb.[10] The sen-

TABLE I. CASES OF TRAUMATIC VULVAR HEMATOMA REPORTED IN THE LITERATURE BETWEEN 1887 AND 1919

AUTHOR	YEAR REPORTED	NO. OF CASES
1. Himmelfarb[20]	1887	1
2. Felkin[16]	1888	1
3. Page*	1889	3
4. Ligternic*	1889	1
5. Hoedmaker[25]	1890	4
6. Steiner[44]	1890	1
7. Pate*	1890	1
8. Vinay	Collected by Ohnaker up to 1911	2
9. Veit		1
10. Walther		2
11. Merkertschiantz		1
12. Neugebauer		1
13. Winkel		1
14. Theim		1
15. Hirst[21]	1896	1
16. Brickerer[5]	1896	1
17. Bonnet-Laborderie[4]	1902	1
18. Frank-Kamenetzky[15]	1909	12†
19. Ohnaker[35]	1911	3
20. Reich[38]	1911	4‡
21. Benestad[3]	1914	1
22. Ohnan[34]	1914	2

*Collected by Ohnaker (1911).[35]

†Collected by Frank-Kamenetzky (1909).[15] Cases listed more completely by Ohnaker also duplicated here with insufficient data.

‡Collected by Reich (1911).[38]

TABLE II. CASES OF TRAUMATIC VULVAR HEMATOMA REPORTED IN THE LITERATURE BETWEEN 1920 AND 1953

AUTHOR	YEAR	AGE	TRAUMA	SIZE	TREATMENT
1. Jacobi and Rexilius[26]	1920	—	Fell from scaffold	Man's fist, left labium	1. Immediate incision and packing of wound with gauze 2. Ligated vessel to clitoris
2. Wachtel[46]	1928	28	Struck sharp edge on wagon	Baby' head	1. Immediate incision and packing with gauze
3. Nowosielski and Uhm[33]	1931	35	Kicked by husband	Large, entire right labium to buttock	1. Conservative, ruptured spontaneously on sixth day with abscess formation
		22	Kicked by husband	Man's fist, right labium	1. Conservative, discharged on sixteenth day
4. Rin[41]	1941	17	Fell in bathtub	Hen's egg, left labium	1. Conservative, with aspiration on fifth day
5. Pihlamaa[37]	1950	20	Fell against toilet seat	3 man's fists, left labium	1. Conservative at first, incision with removal of clots on third day
6. Campbell[7]		18 Mo.	Fall causing straddle injury	Entire right labium to abdomen	1. Conservative with dilatation of urethra because of urethral injury
7. Dlhós[13]	1952	19	Coitus	Grapefruit sized	1. Conservative for 4 days, then incision with removal of clots 2. Patient received vitamin K and calcium

sory nerve supply is derived from the pudendal nerve, the perineal nerve to the vulva and perineum, and the dorsal nerve to the clitoris.[27] Those interested in anatomic details of this region are referred to the atlas written by Anson.[1]

A hematoma is defined as a tumor containing effused blood.[14] This blood, resulting from the rupture of a blood vessel or vessels, collects in the perigenital tissue,[47] and tends to follow the natural cleavage lines of the connective tissue and fascia.[31] The hematoma may attain considerable size before it stops growing, because the loose subcutaneous tissue affords little resistance until the mass is fairly large.[9]

Trauma

The type of trauma sufficient to cause hematoma formation can vary from a simple fall to the unusual, i.e., a human bite[20] (Table III).

Accidents in which the patient falls against sharp or blunt objects and straddle injuries constitute the major types of trauma responsible for the formation of hematomas.

It is of interest to note that, in 40 cases, 28 (70 per cent) of the hematomas occurred in the right labium, 10 (25 per cent) occurred in the left labium, and 2 (5 per cent) were bilateral. The age range in these cases was from 18 months to 49 years.

TABLE III. TYPES OF TRAUMA RESPONSIBLE FOR FORMATION OF HEMATOMAS IN 30 CASES

TYPE OF TRAUMA	NUMBER OF CASES	%
1. Fall against a sharp object	12	40.0
2. Straddle injury	6	20.0
3. Coitus	4	13.3
4. Kick to labia	3	10.0
5. Fall in bathtub	2	6.6
6. Other, i.e., gorged by bull's horn, sleigh riding	2	6.6
7. Human bite	1	3.3

Classification of Traumatic Hematomas

The usual classification used by Jacobi and Rexilius[26] and Marcel and Fabre[30] has been simply small hematomas and large hematomas. Other descriptive terms have been used, including man's fist,[33] coconut,[12] grapefruit,[13] and sausage shaped.[39] It is agreed that these terms lack uniformity and scientific accuracy. It is very difficult when dealing with a condition which is subject to wide variation and subsequent changes to obtain a description of pin-point accuracy. One could measure the longitudinal and transverse diameters of the hematoma as was done in one case by Ohnaker,[35] but such highly accurate measurements are not necessary. From a clinical viewpoint and for uniform descriptive purposes it is well to have a general although simple type of classification. Since the size of the vulvar hematoma has a definite bearing on the initial and later course of treatment, an arbitrary descriptive grouping based on initial or developed size is suggested. Traumatic vulvar hematomas may be placed in three groups, small, medium, or large. The small hematomas are approximately the size of a hen's egg as suggested by other authors.[26, 30, 46] The medium-sized hematomas are the size of an orange. The large hematomas are the most extensive. These may extend from the mons veneris to the buttock or rectum. These are described as being the size of a grapefruit[12, 13] or larger.[33]

Diagnosis

Diagnosis can be easily made. The patient usually presents herself for treatment within a few hours after trauma to the labia. She will state that on examination she noticed a discolored swelling in the injured area. She will complain of severe pain which is made worse upon walking or standing. Some complain of inability to void or a fear of voiding, which upon questioning will be found to be due to the location of the hematoma in the path of the urinary stream. Also they complain of severe pain on pushing the hematoma to one side in order to void.

Examination will reveal a bluish, tense, exquisitely tender swelling in the affected labium which may or may not occlude the vaginal orifice or urethra, depending upon its size. Photographs depicting the physical appearance of traumatic vulvar hematomas may be seen in the writings of Hirst,[21, 22] Rin,[41] Wachtel,[46] Dlhós,[13] and Campbell.[7]

Case Reports

The following cases were treated on the Gynecological Service during the period from November, 1949, to February, 1954.

CASE 1.—No. 84168. R. E., a 20-year-old Negro woman, was admitted on Nov. 24, 1949, three hours after she slipped and fell against the edge of an open dresser drawer. Immediately, she experienced a sharp pain in the right labium. Upon examination she noticed a large bluish mass which increased in size during the next few hours. The hematoma was aspirated and bright red blood was obtained. It was large (the size of a baby's head), involving the entire right labium majus, labium minus, part of the clitoris, and the vaginal wall. Penicillin was ordered, with warm boric acid compresses.

The hematoma increased in size, so on the fourth day it was incised. Dark clots were removed and the incision was closed without drainage. The patient was discharged on Nov. 30, 1949, the second postoperative day.

On Dec. 7, 1949, follow-up examination showed a swelling the size of a lemon. The incision was partially opened and blood clots removed. The patient was advised to apply hot compresses. By Jan. 7, 1950, the wound had healed sufficiently so that she was able to return to work.

Comment.—This case serves to illustrate several major points of what not to do in the emergency treatment of traumatic hematomas. (1) No hematoma should be aspirated during the formative period (first 12 to 24 hours) and certainly not within 3 hours after injury. The effused blood exerts a tamponade effect upon the blood vessels responsible for the hemorrhage. This causes pressure thrombosis and obliteration of small bleeding vessels, resulting in cessation of bleeding, and checks further expansion of the hematoma. Release of this tamponade by aspiration can cause the bleeding area to open again and continue bleeding, causing the hematoma to grow larger. Thus by premature aspiration, a hematoma which would have remained small and innocuous becomes a large one requiring complicated treatment. (2) Ice in some form should be applied to the affected area for the first 24 hours. Cold causes a local hypothermia with a resulting decrease in blood flow to the area. Warm dressings conversely cause an increase in blood flow locally by causing dilatation of the capillary bed. This of course is not desirable during the first 24 hours. (3) An external pressure dressing is instrumental in controlling hemorrhage, by pressure alone. No pressure dressing was applied to the hematoma. (4) The patient was operated upon after improper handling during the emergency period. The hematoma partially recurred, presumably because she was permitted full activity too soon after operation. This recurrence added to the patient's disability and discomfort.

CASE 2.—No. 114381. M. S., a 45-year-old white woman, was admitted on Nov. 13, 1952, one hour after she lost her balance and fell from a ladder and struck the pudendal-perineal region against the back of a chair (straddle injury). She immediately experienced pain in this region and upon examination noticed a large hematoma (the size of a grapefruit) covering the right labium. She applied ice to the area and came to the hospital.

After laboratory studies had been done, she was examined under general anesthesia. The hematoma was large (the size of a melon) and increasing in size. It involved the entire right labium majus, minus, clitoris, and vaginal wall. An incision was made into the hematoma and several pints of clots were removed. Interrupted figure-of-eight mattress sutures were inserted into the oozing bed of the hematoma. Four strips of absorbable gauze were also applied to the oozing surface. The wound was closed without drainage. A transfusion of 500 c.c. of whole blood was given. The vagina was firmly packed, and a pressure dressing was applied.

Postoperatively, penicillin and streptomycin were given for 3 days. An ice bag was applied. The vaginal pack was removed in 24 hours and perineal care instituted. X-rays of the pelvis showed no fractures. The Foley catheter was removed on the fifth day. The patient was discharged on the thirteenth postoperative day. The wound was healed. A follow-up examination in 7 days showed ecchymosis to be present.

Comment.—Proper treatment instituted early reduced the patient's discomfort and period of disability. She was incapacitated for a period of 20 days in contrast to 44 days in Case 1.

CASE 3.—No. 117491. L. Z., an 18-year-old white girl, slipped on March 6, 1953, and struck the right labium against the sharp corner of a table at 6 P.M. while at work at the hospital. Immediately she noted pain in the labium. She was treated in the emergency room within 30 minutes after injury. Examination showed that the hematoma was small (the size of a walnut). She was sent home with codeine sulfate and told to apply ice. She returned 3 hours later complaining of severe pain made worse on standing and walking, along with a fear of voiding.

Examination showed that the hematoma had progressed to medium size (the size of an orange). Upon admission a compression dressing was applied along with cold compresses. The hematoma did not appear to be growing larger, so conservative treatment was continued. During her hospital stay, she had to be catheterized several times because of difficulty in voiding. Following discharge, the hematoma had reabsorbed so that on examination 5 days later only a small ecchymotic area remained.

Comment.—This case illustrates the fact that traumatic hematomas when seen soon after the trauma may be small, but they can enlarge rapidly within a few hours. Therefore, all patients with hematomas, regardless of initial size, should be admitted to the hospital for observation and treatment.

CASE 4.—No. 119597. T. E., a 23-year-old Negro woman, was admitted on April 13, 1953, after she had been attacked by an overly amorous man and kicked in the pudendal region. She came to the hospital because she could not void. She was given morphine sulfate and examined. The hematoma was large (the size of a grapefruit), completely occluding the vaginal orifice. It involved the left labium majus, minus, clitoris, urethral mucosa, perineum, and perianal region. No other injuries were found. The hematoma was very tender and painful.

A Foley catheter was inserted into the bladder and 700 c.c. of clear urine was obtained. The hematoma though large appeared stationary, so conservative treatment was instituted. A pressure dressing and ice were applied. Perineal care was begun 24 hours later. Frequent observations of the hematoma showed that it did not increase in size. Penicillin and streptomycin were given for 3 days. On the third day a small necrotic area about 1 cm. in diameter appeared on the vaginal mucosa over the maximum protrusion of the hematoma.

The catheter was removed on the seventh day and the patient was discharged on April 24, 1953. The hematoma opened spontaneously 13 days after formation while she was in the tub and drained some clots. Examination showed no active bleeding or infection. The wound healed in 7 days and ecchymosis was present for 10 more days.

Comment.—This hematoma would have been treated best by performing an elective incision on the fifth or sixth day following the original injury. This would have speeded up resolution as well as decreased the period of disability.

CASE 5.—No. 125223. L. S., a 32-year-old white woman, was admitted 3 hours after trauma to the right labium when she lost her balance while trying to catch a dog and fell against a small garbage can. Pain and swelling were noted immediately after the accident (6 P.M.). She developed difficulty in voiding within 3 hours (9 P.M.) so she sought medical aid.

She was taken to the operating room and under general anesthesia the pudenda and surrounding areas were examined. A Foley catheter was placed into the bladder and clear urine obtained. A hematoma (the size of a lemon) was present in the right labia, minus and majus. There were also some redness and edema about the urethral orifice. The hematoma appeared to be stationary so conservative treatment was instituted. On examination 10 days after discharge, a fluctuant mass was present. This was aspirated and semiclotted blood obtained. Complete resolution occurred within 7 days.

CASE 6.—No. 126905. E. T., a 19-year-old Negro girl, was admitted four days after she had fallen while roller skating and slid along the floor causing trauma to the right labium minus. Immediately after the accident she had no symptoms. The next morning she developed a dull ache in the labium minus. She remained in bed for three days until she was brought to the hospital.

The hematoma was small (the size of a golf ball). Conservative treatment was carried out. Five days after the accident the hematoma was aspirated. Penicillin was placed into the hematoma cavity after 15 c.c. of blood was removed. Follow-up examination 7 days later showed almost complete resolution.

Comment.—Aspiration of small hematomas on the fourth or fifth day will speed up the process of reabsorption. Injection of hyaluronidase may take the place of aspiration, as this is said to hasten absorption by virtue of its spreading properties.[43]

Treatment

Jacobi and Rexilius, Wachtel, and Marcel and Fabre outline the therapy of traumatic hematoma as either conservative or operative.

The consensus[9, 26, 30, 46] on this subject is that small hematomas are best treated conservatively with bed rest, elevation of the hips, cold packs, and compression dressing. These hematomas usually reabsorb without complications. If infection and abscess do occur, however, incision and drainage, culturing, and sensitivity tests are carried out and the use of the most specific agent available is indicated.[29]

Ohnaker, Jacobi and Rexilius, and Wachtel feel that all large hematomas should be treated by operative means immediately after the hematoma has formed. They state that their reasons are to prevent anemia, infection, and abscess formation.

Nowosielski and Uhm,[33] on the other hand, treated two large hematomas conservatively. One ruptured and drained on the sixth day with formation of an abscess. The other reabsorbed without any difficulty. Dlhós, Hoedmaker, and Pihlamaa treated their cases conservatively first, then by elective surgery on the third or fourth day following the formation of the hematoma. These forms of therapy do not consider the rapidly enlarging hematoma nor the large hematoma which is several days or more old when first seen.

On the basis of the opinions of these writers and the experience gained in the treatment of the cases outlined previously, the following program is presented, which is applicable to the treatment of all sizes of hematomas.

General Considerations.—

1. Upon admission to the hospital, a complete blood count, type, and cross-match for whole blood, x-rays of the pelvis (when indicated), as well as a general history and physical examination, are done.

2. Every patient should be examined under adequate sedation or light general anesthesia (preferred). This cannot be overemphasized, as these hematomas are extremely tender and the area cannot be examined if the patient becomes uncooperative because of pain.

a. The exact extent of the hematoma is carefully observed along with the condition of the vaginal wall, urethra, and clitoris.

b. All vaginal or vulvar lacerations are cleansed, débrided, and sutured immediately.[33]

c. The anus and rectum are inspected for any possible injury. Untreated perforations of the extraperitoneal rectum and anal region can have a serious outcome.[32]

d. A check is made for possible fracture of the pelvis. Palpation of the symphysis pubis or the ischium on rectal examination may disclose an irregularity indicative of a fracture.[40]

e. An indwelling catheter is inserted in every case for at least 24 hours or longer as necessary. The following reasons are given for this: (1) A catheterized specimen can be obtained with minimal discomfort. With a catheter in position, a cystogram[36] can be taken to check on any possible injury to the bladder. (2) There may be some direct injury to the urethra as a result of the trauma. Edema or extension of the hematoma may later occlude the urethral orifice, causing mechanical anuria. This can be prevented by maintaining a patent urinary pathway by early insertion of an indwelling catheter. (3) With the catheter in position a firm compression dressing can be easily applied.

3. If, at this initial examination, the hematoma is enlarging rapidly and other signs of blood loss are present, exploration for a possible source of large arterial bleeding should be made. The clitoridis artery and its branches may be the primary source of hemorrhage.[26]

4. If no surgery is to be done, a compression dressing is applied. A broad T binder with V pads or sponge rubber may be used. Preferably a hip spica elastic dressing[39] composed of a broad (4 or 5 inch) elastic bandage over the V pads or sponge rubber can be snugly applied. A counterpressure vaginal pack may be inserted.[24]

5. Ice bags should be applied for the first 24 hours. Perineal care is then instituted using warm boric acid dressings or a heat lamp.

6. In order to make the patient more comfortable a pillow can be placed under the hips and knees.[9]

7. Frequent observations as to the progress of the hematoma should be made by the observer who originally saw the patient. If it appears to be expanding rapidly, surgical exploration is carried out immediately.

Surgical Procedure.—

1. An adequate incision is made into the hematoma. Whether this is made over the point of maximum bulging or at the mucocutaneous junction or through the vaginal mucosa[24] is immaterial, as the end results are the same.

2. All bleeding caused by the incision should be controlled. All blood clots are removed to visualize the depths of the wound. All active bleeding

points are clamped and ligated. On entering the hematoma one should not be alarmed that a large amount of blood is present, as this is the usual state of affairs.

3. In most cases, only a diffusely bleeding surface will be found. Interrupted figure-of-eight, or other mattress sutures are placed to control this bleeding.

4. Topical thrombin* is then sprayed onto this oozing surface, or the powder form may be applied to effect hemostasis.[43] If the hemostasis obtained in this manner is not satisfactory, absorbable gauze plain or saturated in thrombin solution, is packed or sutured against the bleeding surface. It has been stated that occasionally this material may cause a persistent discharge from the wound by failure to absorb.[11] This is probably due to the use of too much gauze.

5. The wound is closed in an anatomic fashion. Marcel and Fabre advise leaving the suture ends long upon closing the incision, so that a gauze roll can be tied against the incision for compression. The wound can usually be closed without drainage. If drainage is desired, a small Penrose drain may be placed in the lower portion of the incision and removed in 24 hours.[18]

6. Routine packing of the cavity with iodoform gauze, following the evacuation of the blood clots has been suggested by Ohnaker, with plain gauze by Jacobi and Rexilius, and with snake-venom gauze by Hannan. They advocate gradual removal of the packing in stages after it has been in position for 24 to 48 hours. The procedures outlined in 2, 3, and 4 above are adequate to control the bleeding and do not have the added risk of secondary hemorrhage often noted on removal of the packing. As a desperate emergency measure to control bleeding in large hematomas, packing with gauze is a desirable measure.

7. Blood transfusions should be given as determined by the erythrocyte count, hemoglobin and hematocrit determinations, as well as the condition of the patient.

8. Koagamin† (parenteral coagulant) may be given during the first 24 hours postoperatively for its theoretical effect on blood coagulation.[42]

9. Broad-spectrum antibiotics are given for 3 days prophylactically. After this time, antibiotics are given as the need arises.

10. The procedures outlined under Nos. 4, 5, and 6 of General Considerations are also carried out.

Medium-Sized Hematomas.—

These may be treated conservatively if stationary. In order to hasten resolution, however, one can aspirate or make a small incision into the hematoma under local anesthesia on the fourth or fifth day. Penicillin may be instilled into the hematoma cavity.[19] Lamm and Lamm feel that the incidence of infection following aspiration may be significant. This was not observed by us or by others.[6, 41] It is of interest to note that of all the cases in the literature, an abscess developed in only one, that of Nowosielski and Uhm. Therefore, it seems that this complication is not common. To facilitate dissolution of clotted blood by enzymatic débridement, streptokinase and streptodornase may be used.[8]

Large Hematomas.—

If these hematomas are first seen 24 hours or more after formation and show no further expansion, there is no harm in continuing conservative treatment for 4 or 5 days. During this time the hematoma will undergo resolution

*Thrombin, Topical (bovine origin) manufactured by Parke, Davis & Company, Detroit Mich.

†Koagamin, aqueous solution of oxalic and malonic acids manufactured by Chatham Pharmaceuticals, Inc., Newark, N. J.

and organization and the vessels responsible for the bleeding will be thrombosed. Elective surgery can be easily performed and secondary hemorrhage should not occur. By treating large hematomas so, rather than conservatively, perforation with possible abscess formation can be prevented.

Prognosis, Complications, and Associated Injuries

Prognosis in traumatic vulvar (nonpuerperal) hematomas is very good. Healing occurs with minimal complications (Table IV). No fatality was noted in the cases reported in the literature. However, Jacobi and Rexilius quote Hoffman as having seen a case which caused death in a child.

TABLE IV. COMPLICATIONS ENCOUNTERED IN 16 CASES OF TRAUMATIC VULVAR HEMATOMA

COMPLICATIONS, ASSOCIATED INJURIES, AND MEDICAL CONDITIONS	NO. OF CASES
1. Wounds of the vagina or labia	8
2. Recurrence (partial) of hematoma	2
3. Urethral injury	2
4. Formation of abscess of labium	1
5. Fracture of pelvis	1
6. Epilepsy	1
7. Hemophilia	1

Associated wounds of the labia and vagina are most common. These must be adequately treated and not considered as trivial injuries. A fatality due to a slight wound of the labium has been reported by Ford.[17]

Summary

1. Traumatic vulvar hematomas are painful and disabling, and must receive prompt, active treatment in order to minimize discomfort and possible complications.

2. Six additional cases have been presented along with a review of the literature since 1887.

3. A program of therapy has been presented by which they can be treated satisfactorily.

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CLINICAL EXPERIENCES WITH THE SKIN BIOPSY METHOD OF DETECTING CHROMOSOMAL SEX

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BY MEANS of nuclear microscopy, Barr and his associates[1-9] have made an impressive and unique contribution to sex identification. Basing their work on observations in experimental animals[1-4] and human beings,[5-9] these investigators have demonstrated the feasibility of detecting the chromosomal sex of an individual by means of a skin biopsy. Differences in epidermal nuclear morphology permit ready differentiation between chromosomal males and females.

Briefly stated, these workers have described a sex difference in intermitotic nuclear structure in the cells of various tissues and organs of numerous animal species and humans. A conspicuous mass of chromatin, termed "sex chromatin" by them, is found in approximately two-thirds of the cells of females. In human epidermal nuclei,[5] the sex chromatin is approximately one micron in size and is planoconvex with its flattened aspect in contact with the inner surface of the nuclear membrane. Its size, shape, and position usually distinguish it readily from other particulate chromatin material as well as from the nucleolus. A smaller chromatin body, lacking the characteristic size and morphology of the "female" sex chromatin, may be encountered very infrequently (approximately 5 per cent) in cells of males. Moore and Barr[6] have summarized the evidence indicating that fusion of portions of two X chromosomes of female cells results in the formation of a distinctive chromatin body, the sex chromatin. It is thought that the relatively small size of the Y chromosome may account, in part, for the failure of the XY complex of the male cells to produce a chromatin mass of comparable size.

These fundamental observations have been confirmed by Hunter, Lennox, and Pearson[10] and by Marberger and Nelson.[11] Barr and his colleagues have applied their work to patients with hermaphroditism[5, 7] and transvestism[9] and Polani, Hunter, and Lennox[12] and Wilkins, Grumbach, and Van Wyk[13] have reported their findings in individuals with ovarian agenesis.

The present study was undertaken in an effort to explore the usefulness of the skin biopsy method of chromosomal sex detection by applying it to a variety of clinical states. These included individuals with sex hormonal disturbances, intersexual abnormalities, cryptorchidism, and adrenocortical disorders. A much larger group of sexually and hormonally normal males and females served as controls.

Material and Methods

Only living patients were utilized, portions of skin being obtained in most instances during the course of an unrelated surgical procedure and in the remainder by punch biopsy. The control series consisted of 28 males and 27 females, ranging in age from the newborn to 84 years. As far as could be determined, these subjects manifested no sexual or hormonal abnormality which was not physiological for their respective ages.

Composing the first group were 21 individuals (Table I). Fourteen of these had been subjected to abnormal sex hormonal influences, two were patients with intersexuality (hermaphroditism or pseudohermaphroditism), one was a pubescent male with uncomplicated unilateral cryptorchidism, two were patients with Cushing's syndrome and two had Addison's disease. It was felt that identification of chromosomal sex in these patients might serve a dual purpose; first, to learn whether the sex chromatin can be influenced by endogenous or exogenous alteration of the sex hormonal status or by serious aberrations in the metabolism-regulating functions of the adrenal cortex; second, to elucidate the chromosomal, and possibly the genetic, basis for certain congenital sexual abnormalities.

TABLE I. SEX TYPE OF EPIDERMAL NUCLEAR MORPHOLOGY ENCOUNTERED IN PRESENT STUDY

PATIENTS	NO. OF CASES	NUCLEAR MORPHOLOGY (NO. OF CASES)	
		FEMALE	MALE
I. Female.—			
A. Normal	27	F (27)	
B. With virilism			
1. Endogenous			
a. Stein-Leventhal syndrome	3	F (3)	
b. Adrenogenital syndrome	1	F	
2. Exogenous			
a. Testosterone propionate therapy for mammary carcinoma	1	F	
C. With estrogen deficiency			
1. Endogenous			
a. Ovarian agenesis	1		M
2. Exogenous			
a. Prepuberal hypogonadotropic eunuchoidism (induced by radiotherapy)	1	F	
D. With Cushing's syndrome	1	F	
E. With Addison's disease	1	F	
II. Male.—			
A. Normal	28		M (28)
B. With androgen deficiency			
1. Endogenous			
a. Congenital testicular deficiency	2		M (2)
2. Exogenous			
a. Castration plus estrogen therapy for prostatic carcinoma	3		M (3)
b. Estrogen therapy for prostatic carcinoma	1		M
C. With cryptorchidism (unilateral uncomplicated)	1		M
D. Receiving combined androgen and estrogen therapy	1		M
E. With Cushing's syndrome	1		M
F. With Addison's disease	1		M
III. Intersexual.—			
A. Male pseudohermaphrodite	1		M
B. Male pseudohermaphrodite or true hermaphrodite	1		M
Total	76		

Skin specimens were treated according to the procedure described by Moore, Graham, and Barr.[5] After fixation in modified Davidson's solution for 24 hours, they were immersed in 70 per cent alcohol with frequent washings for approximately two days. Thin paraffin sections were stained with hematoxylin and eosin and examined under oil immersion.

No attempt was made to compute the exact percentage of nuclei containing the sex chromatin. This was found to be unnecessary in view of the ease with which a preponderance or virtual absence of typical sex chromatin could be determined after careful study of many fields. Technically imperfect preparations lacking fine nuclear detail were discarded. Satisfactory specimens from a total of 76 patients were studied.

To ensure freedom from prejudice in the interpretation of nuclear morphology, all slides were assigned a code number so that the sex of the patient in each instance was unknown to the examiner. The sex type of nuclear structure was then recorded in "blindfold" fashion by the authors independently of one another. The results obtained by one observer were checked against those of another and then compared with the master list of known sexes. The independent findings of each worker coincided in all instances. Full agreement with the master list was recorded in all cases except one which is discussed hereafter.

Results

Sex chromatin, a characteristic planoconvex body lying against the nuclear membrane, was identified in the majority of epidermal nuclei (Fig. 1) of all 27 normal female control patients (Table I). In sharp contrast, the nuclei (Fig. 2) of 28 normal males only rarely contained a chromatin mass resembling the sex chromatin and were, therefore, uniformly of the male type. In certain patients subjected to gynecological surgery, biopsy of the vaginal epithelium was also performed. Female nuclear morphology was distinguished in this material as readily as it was in the epidermis. An incidental observation was the fact that the epithelial nuclei of hair follicles and sebaceous glands encountered in skin biopsy sections also exhibited corresponding sex differences. Similar findings in numerous different human tissues and organs have been reported recently by Moore and Barr.[6]

Female nuclear morphology was found in three virilized young women whose ovaries at operation revealed the characteristic lesions of hyperthecosis (Stein-Leventhal syndrome).

Nuclear structure of the female type was also observed in a 16-year-old girl with virilization due to postpuberal adrenocortical hyperfunction, probably the result of bilateral adrenocortical hyperplasia. For the previous two years, this patient manifested acne, generalized hirsutism, and oligomenorrhea. The 24 hour urinary excretion of neutral 17-ketosteroids was 20.9 mg.

A 40-year-old woman with masculinization resulting from prolonged testosterone propionate therapy (300 mg. per week for two months) for inoperable mammary carcinoma similarly showed the female type of nuclei.

The epidermal nuclear morphology of a 43-year-old woman with ovarian agenesis (Turner's syndrome) was of the male type. Although the clinical diagnosis had not been verified by abdominal exploration, the evidence supporting this diagnosis is firm. This patient manifested primary amenorrhea, shortness of stature, cubitus valgus, and failure of development of secondary sex characteristics. Hair was scant in the pubic region and absent in the axillae. The urinary gonadotropin excretion, determined five years previously at the age of 38 years, was increased (assay positive at 90 mouse uterine units; higher levels not tested). Roentgen examination showed

diffuse osteoporosis. Pneumogynecography disclosed the presence of a small uterus but no ovarian structures could be identified. Cyclic estrogen therapy, productive of withdrawal bleeding and slight breast development, had been administered for 11 months prior to the date of the skin biopsy.

The female type of epidermal nuclei was observed in a 17-year-old girl with diabetes insipidus and hypogonadotropic hypogonadism of prepuberal onset. She had a eunuchoidal habitus with marked evidence of estrogen deficiency and had been receiving cyclic estrogen therapy for 14 months. Adenohypophyseal gonadotropic function had been impaired during childhood by roentgen radiation to the pituitary region because of a diagnosis of optic glioma.

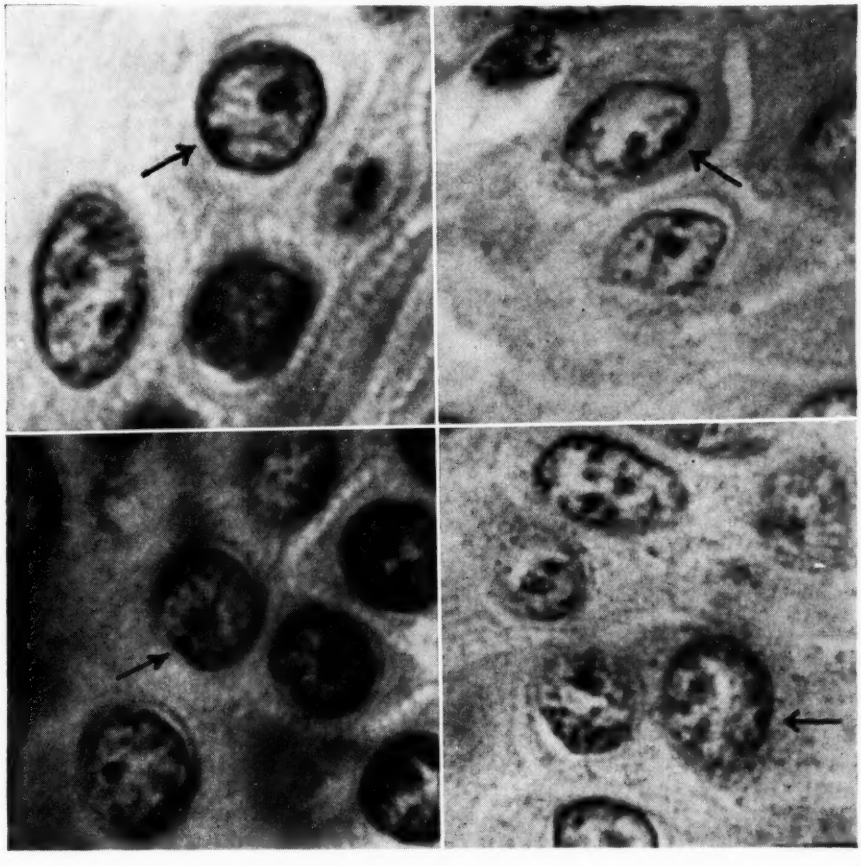

Fig. 1.—Human epidermal nuclei in the female showing typical sex chromatin masses (arrows). In each instance the flattened aspect lies in contact with the nuclear membrane. (Hematoxylin and eosin. ×1500.)

It is appropriate to remark at this point that several instances of physiological ovarian estrogen deficiency are necessarily included in the control group of normal females. This applies to subjects of prepuberal and postmenopausal age.

The epidermal nuclear morphology of all six men with marked evidence of hypogonadism was of the male type. Two of these patients, previously reported,[14] had untreated congenital familial testicular deficiency and four had been receiving 2 to 3 mg. of diethylstilbestrol daily for prolonged periods

of time for inoperable prostatic carcinoma. Three of these had also been subjected to bilateral orchiectomy six months to three years previously. Gynecomastia was present in each of the six patients.

The male type of nuclear structure was likewise found in a 15-year-old boy with uncomplicated, unilateral cryptorchidism and in a 60-year-old man who had been taking methyltestosterone, 10 mg., and diethylstilbestrol, 0.5 mg., daily for 6 months.

Epidermal nuclear morphology of the male type was identified in an intersexual child 18 months of age. At birth the external genitals were found to be compatible with either male or female pseudohermaphroditism or even true hermaphroditism. Repeated determinations of the 24 hour urinary excretion of neutral 17-ketosteroids showed no elevation indicative of adrenal cortical hyperfunction. Prior to exploratory operation, a skin biopsy indicated the chromosomal sex to be male, suggesting male pseudohermaphroditism as the most likely diagnosis. At laparotomy, gross and histological examination of the intra-abdominal gonads confirmed this impression.

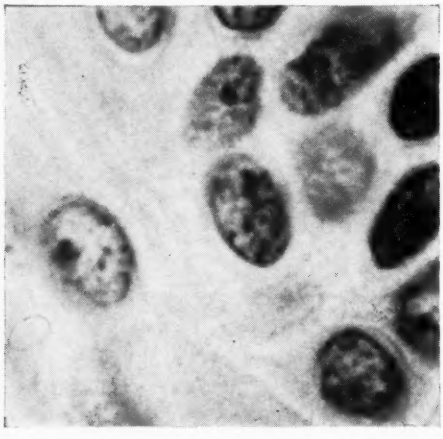

Fig. 2.—Human epidermis showing male type of nuclear structure. Typical sex chromatin bodies are absent. Smaller, nondescript chromatin particles, occasionally lying against the nuclear membrane, lack the well-defined characteristics of sex chromatin. (Hematoxylin and eosin. ×1500.)

The male type of nuclei was also encountered in a 13-year-old intersex who had been reared as a girl and was receiving estrogen therapy at the time of the skin biopsy. Surgical exploration (prior to the beginning of estrogen therapy) disclosed the presence of pelvic gonads with the gross appearance of testicles. Microscopic examination of the gonads revealed them to consist almost entirely of immature seminiferous tubules. However, scattered small foci of apparently characteristic ovarian stroma were also present. The resemblance to ovarian stroma was strengthened by the presence of hilus cells in proximity to nonmyelinated nerve fibers. There were no other structures such as oögonia, ova, or follicles, however, to indicate a truly ovarian component. Although the gonads were predominantly testicular in character, the possibility that they might be ovotestes cannot be entirely excluded. In this event this intersexual patient would be a true hermaphrodite rather than a male pseudohermophrodite.

The chromosomal sex was in agreement with the physical sexual characteristics in a 15-year-old boy with cryptorchidism, in a 30-year-old man and a 46-year-old woman with Cushing's syndrome, and in a 23-year-old man and a 59-year-old woman with Addison's disease. The patients with Cushing's

syndrome presented classical clinical findings and their condition was progressively deteriorating. The 24 hour urinary excretion of neutral 17-ketosteroids and 11-oxygenated steroids was 29.5 mg. and 6.4 mg., respectively, in the man and 10.2 mg. and 3.2 mg., respectively, in the woman. The male patient had been subjected to unilateral adrenalectomy and pituitary irradiation and had been receiving 25 mg. of methyltestosterone daily for 6 months prior to the skin biopsy. The female patient had received pituitary irradiation alone. The Addisonian patients also manifested the characteristic clinical picture as well as electrolyte disturbances. Both of these individuals had been receiving desoxycorticosterone trimethylacetate with good effect.

Comment

The results of the studies of nuclear structure confirm the original observations of Barr and his associates. A difference in intermitotic nuclear morphology, according to sex, was demonstrated in 28 male and 27 female patients who were sexually and hormonally normal. The differentiation hinges upon the presence in female nuclei and virtual absence in male nuclei of a characteristic mass of chromatin, the sex chromatin. During the course of this investigation similar confirmation was reported by Hunter, Lennox, and Pearson[10] and by Marberger and Nelson.[11]

Although there is strong inferential evidence to support the belief that the sex chromatin is produced by fusion of heterochromatic portions of the two X chromosomes of female nuclei, absolute proof is still lacking. Marked endogenous and exogenous alterations in the sex hormonal status of an individual did not influence the incidence or morphology of the sex chromatin. This was true of females with virilization and of those with ovarian estrogen deficiency. It also applied to males with androgen deficiency as well as to those subjected to the feminizing effects of estrogen administration. These observations attest to the stability of the sex chromatin, suggesting that the latter is of chromosomal origin and not an index or effect of the sex hormonal status. These findings are also consistent with the recently published data of Barr[7] who demonstrated female nuclear structure in the epidermal cells of each of 12 female pseudohermaphrodites with adrenocortical hyperfunction.

The present studies in human beings are compatible with previously reported data derived from the experimental animal. Graham[15] described typical differences in the nuclear structure of the embryonic membranes of cat embryos prior to differentiation of the gonads into ovaries or testes. Attempts by Lindsay[16] to modify the sex chromatin of cats by gonadectomy and by the administration of hormones of the opposite sex were unsuccessful.

Our observation of the male type of nuclear morphology in a patient with ovarian agenesis (Turner's syndrome) is of great interest. While this work was in progress, Polani, Hunter, and Lennox,[12] reported the male type of epidermal nuclear structure in each of three such patients studied by them. Shortly afterward, Wilkins, Grumbach, and Van Wyk[13] published their results in eight patients with the same disorder. The epidermal nuclear morphology was of the male type in six individuals, and of the female type in two.

The possibility that certain females with Turner's syndrome may be chromosomal males was suggested by Jost.[17] In earlier studies[18, 19] employing placental mammals, this investigator found that effects of early castration in rabbit fetuses differed according to sex and according to whether gonadectomy was performed before or after genital tract differentiation. In cases of females, fetal ovariectomy does not inhibit female organogenesis. Oddly enough, development into females also occurs when male embryos are castrated prior to differentiation of the genital tract. Similar observations in the mouse have been recorded by Raynaud and Frilley.[20]

The problem of underlying hormonal mechanisms is not germane to the present discussion. Nevertheless, these observations are significant in that they demonstrate the fact that under certain circumstances chromosomal and genetic sex may be opposite to that of the apparent genital sex. The experimental and clinical data strongly suggest that at least some patients with Turner's syndrome are genetic males. Such individuals would actually represent instances of testicular rather than ovarian agenesis.

Gonadal developmental defects may play a role in the pathogenesis of other congenital sexual abnormalities, notably true hermaphroditism and certain types of pseudohermaphroditism. The male type of nuclear morphology was demonstrated in an 18-month-old male pseudohermaphrodite. This is in accord with the experience of Barr,[7] who also found the epidermal nuclear structure of 11 male pseudohermaphrodites to be the male type. In the opinion of Jost[21] this form of pseudohermaphroditism may be due to testicular deficiency arising at certain developmental stages. Such deficiency may permit partial differentiation of the fetal female genital tract in the presence of male gonads.

The male type of nuclear morphology in the skin of the 13-year-old intersex is more difficult to evaluate in the light of the anatomical findings in the genital apparatus. The accessory sexual organs were female in type, including Fallopian tubes, uterus, vagina, a moderately enlarged clitoris and a perineal urethra. The gross and histological appearance of the gonads was that of testicles but, as previously described, occasional microscopic foci of apparently characteristic ovarian stroma were present. These were not seen in biopsy specimens obtained during operation but were found in routine sections taken after bilateral gonadectomy.

Were it not for this latter finding, the diagnosis of male pseudohermaphroditism would be tenable and male nuclear structure would be expected. If the gonads are interpreted as ovotestes, this individual would be considered a true hermaphrodite, and the male chromosomal sex in this case may be indicative of the predominant, rather than the true, sex. In this connection it is interesting to note that in four true hermaphrodites, Barr[7] found the nuclear morphology to be female in three and male in one. On the other hand, only male nuclear morphology has been encountered in male pseudohermaphrodites while female pseudohermaphrodites with adrenogenitalism contain the female type exclusively.[5, 7, 22]

The role of the adrenal cortex in the production of certain types of congenital and acquired sexual abnormalities is well known. It is significant, therefore, to note that marked deviations in adrenocortical function, characterized by excesses as well as by deficiencies such as occur in Cushing's syndrome and Addison's disease, respectively, do not influence the sex chromatin.

The results of the foregoing studies support Barr[7] in his contention that the skin biopsy test is helpful in the diagnostic differentiation between female pseudohermaphroditism due to adrenocortical hyperfunction and male pseudohermaphroditism. This applies particularly to newborn and very young infants in whom the clinical findings are likely to be equivocal.

Summary

1. The accuracy and relative simplicity of chromosomal sex detection by means of skin biopsy is confirmed in a study of 28 male and 27 female patients who were sexually and hormonally normal. Sex differences in epidermal nuclear morphology depend upon the presence in females and virtual absence in males of a characteristic chromatin mass, the sex chromatin.

2. Studies of nuclear morphology in the skin of a group of individuals with marked aberrations of sex hormonal status indicate the stability of the sex chromatin in this respect. These observations are consistent with the hypothesis that the characteristic chromatin body is derived from portions of the two X chromosomes of females and that it is not an index of sex hormonal function.

3. The male type of epidermal nuclear structure was encountered in a patient with ovarian agenesis (Turner's syndrome), in one with male pseudohermaphroditism, and in another with either male pseudohermaphroditism or true hermaphroditism. Some pertinent genetic considerations in the pathogenesis of these congenital sexual abnormalities are discussed.

4. The chromosomal sex corresponded to the apparent genital sex in a boy with unilateral uncomplicated cryptorchidism, in a man and a woman with Cushing's syndrome, and in a male and a female with Addison's disease.

5. These studies support the view that the identification of chromosomal sex by the skin biopsy method is helpful in the differentiation between female and male pseudohermaphroditism.

We are greatly indebted to Drs. S. H. Klein, H. E. Leiter, L. Lapid, S. Silverstone, and N. Silver for their generous cooperation in supplying us with some of the skin specimens. We are also grateful to Dr. Lotte Strauss, who supervised the processing of the biopsy specimens, and to Miss Doris Murray for her technical assistance.

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PLASMA CHOLINESTERASE ACTIVITY IN NORMAL PREGNANCY AND IN ECLAMPTOGENIC TOXEMIAS*

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PLASMA cholinesterase (ChE) activity during pregnancy has been found by several investigators[1-3] to be decreased compared to that in the nonpregnant state. Herschburg[4] and Tourtellotte and Odell[2] have reported that plasma ChE activity in toxemia of pregnancy is even lower than in normal pregnancy.

The mechanism by which this reduction of plasma ChE activity is produced in pregnancy has not been elucidated. Tourtellotte and Odell did not detect any enzyme inhibitors in maternal plasma or activators in plasma from nonpregnant individuals to account for the decrease. They suggested the possibilities that it might be related to the hemodilution which normally occurs in pregnancy or that it might represent an expression of altered hepatic function in pregnancy. Studies of the relationship of estrogen to plasma ChE activity in rats by Sawyer and Everett[5, 6] showed that the enzyme activity varied with the presence or absence of estrogen, falling after castration of female rats to the level found in males. Conversely, the administration of estrogen to castrate male rats was followed by a significant increase in plasma ChE activity. Barnes and Epperson[3] were unable to demonstrate such an estrogen-enzyme relationship in human beings.

The present report includes the study of plasma ChE activity of normal nonpregnant females, of normal pregnant women at various periods of gestation and at 6 days and 6 weeks post partum, of women with eclampsia and severe pre-eclampsia, and of the term fetus. The possibility that the variations in plasma ChE activity in pregnancy primarily reflect changes in plasma volume has been investigated.

Methods

Patients from the inpatient and outpatient services of the obstetric division of University Hospitals of Cleveland were studied. Fetal blood was obtained from the umbilical cord at the time of delivery simultaneously with the collection of maternal blood. The nonpregnant women were healthy young adult hospital employees. Venous blood was collected in dried mixed ammonium and potassium oxalates and was at once centrifuged. The plasma was separated and immediately frozen until just before assay.

The ChE activity was measured by the method of Michel.[7] Using acetylcholine as the substrate, the fall in pH per unit time is directly proportional to the plasma ChE activity; the enzyme activity is expressed as pH change per hour. Results with this method have been shown to be comparable to those obtained with manometric techniques.

*This work was supported in part by a grant from the Cleveland Area Heart Society.

Plasma volume was measured with Evans blue dye. Exactly 25 mg. of dye was injected after drawing blood into dried mixed oxalate for the plasma blank; then exactly 10 minutes after the dye was injected another plasma sample was obtained. The optical density due to the dye was measured with the Beckman Model B spectrophotometer. These same plasma samples were used for measurement of ChE activity.

Observations

As shown in Table I, the mean plasma ChE activity of 34 normal young adult nonpregnant women was 0.84 pH unit per hour. A progressive decrease in plasma ChE activity was evident as gestation progressed in normal pregnant women. For the three trimesters of pregnancy the mean ChE activities in pH units per hour were: first trimester 0.80, second trimester 0.72, and third trimester 0.66. The average plasma ChE activity on the sixth postpartum day was 0.74 pH unit per hour and at the sixth postpartum week was 0.83 pH unit per hour.

The mean plasma ChE activities of maternal and fetal plasma in normal cases at the time of delivery were virtually identical, 0.66 pH unit for maternal plasma and 0.65 pH unit for cord plasma. There was not always a close cor-

TABLE I. PLASMA CHOLINESTERASE ACTIVITY IN VARIOUS STAGES OF NORMAL PREGNANCY, IN TOXEMIA OF PREGNANCY, AND IN FETUSES FROM NORMAL AND TOXEMIC WOMEN

DIAGNOSIS	NUMBER	MEAN	STANDARD DEVIATION	PER CENT DIFFERENCE
Nonpregnant women	34	0.84	0.104	—
Normal Antepartum:				
First trimester	13	0.80	0.130	- 5
Second trimester	44	0.72	0.125	-14
Third trimester	49	0.66	0.103	-21
Fetus (term)	15	0.65	0.102	-23
Normal Postpartum:				
6 days	16	0.74	0.135	-12
6 weeks	15	0.83	0.120	- 1
Toxemic:				
Eclamptic	11	0.68	0.190	-19
Pre-eclamptic	17	0.68	0.155	-19
Fetus	5	0.65	—	-23

TABLE II. SIMULTANEOUS CHANGES IN PLASMA VOLUME AND PLASMA CHOLINESTERASE ACTIVITY IN NORMAL AND TOXEMIC WOMEN

PATIENT	WEEKS PREGNANT		PER CENT CHANGE	
	INITIAL	FINAL	ChE	PLASMA VOLUME
K. S.* (1)	28	39	+19	-15
(2)	39	1 year (post partum)	+26	-30
A. C.†	30	2 days later	-20	+17
M. S.‡	2 days (post partum)	9 days	+17	-22
W. B.	26	34	- 5	+ 3
L. T.	26	38	+ 5	- 1
D. A.	28	6 weeks (post partum)	+16	-16
I. S.	28	33	- 3	+ 7
J. B.	25	37	- 6	+ 8
E. W.	36	40	- 2	+ 5
E. G.	36	6 weeks (post partum)	+40	-36

*Pre-eclampsia.
†Antepartum eclampsia.
‡Postpartum eclampsia.

relation between the enzyme activity of maternal and cord plasma from the same case; differences as great as 20 per cent were noted.

The mean plasma ChE activity in 11 cases of eclampsia and 17 cases of severe pre-eclampsia was 0.68 pH unit per hour. The mean ChE activity of cord plasma from 5 of these cases was 0.65 pH unit per hour. In most of the toxemic group serial determinations of maternal plasma activity were made, starting at the time of admission and continuing for as long as 10 days. The minimal value in each case was used for calculating the mean ChE activity. Fluctuations as great as 26 per cent were noted in periods as short as 24 hours. The acute changes in plasma ChE activity were accompanied by similar fluctuations of the hematocrit. The simultaneous variations in plasma enzyme activity and hematocrit in 3 cases of eclampsia and one of pre-eclampsia are shown in Fig. 1.

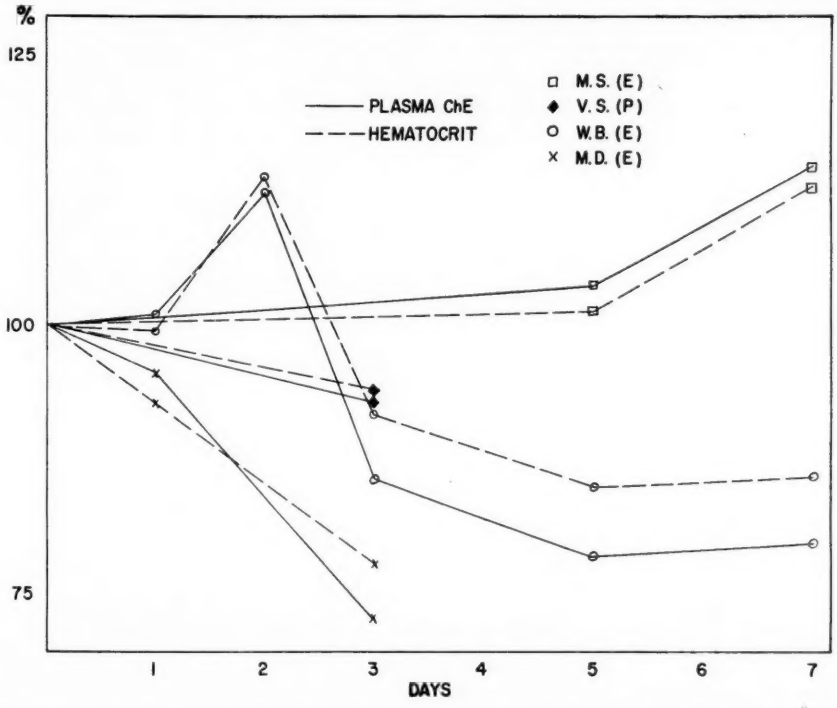

Fig. 1.—Shown are the acute simultaneous changes in hematocrit and plasma cholinesterase activity in cases of toxemia of pregnancy. (P = pre-eclampsia; E = eclampsia.)

Simultaneous measurements of plasma volume and plasma CHE activity were made in 10 women, 7 with normal pregnancies, one with pre-eclampsia, and 2 with eclampsia. Within the limits of precision of measurement the changes in plasma volume and plasma enzyme activity appeared to be inversely proportional. These data are shown in Table II.

Comment

The previous observation that in normal pregnancy plasma ChE activity is lower than in the nonpregnant state has been confirmed. The average decrease in the third trimester of pregnancy was 21 per cent. The degree of decrease in enzyme activity and the time relationship for the appearance of this decrease strongly suggest that the diminution in enzyme activity results primarily from hemodilution since they are similar both in degree and time of onset to the changes in plasma volume during normal pregnancy described

by Dieckmann and Wegner[8] and White.[9] The inverse relationship noted between changes in plasma volume and plasma ChE activity over a period of weeks to months in the same pregnant subject supports this concept.

That plasma ChE activity is further depressed in eclamptogenic toxemia of pregnancy could not be confirmed even though the cases of toxemia studied were severe and included 2 fatal cases.[10] Considerable daily variation in plasma enzyme activity was encountered in many of the toxemic group. Since this acute variation was proportional to fluctuations in hematocrit, it is probable that such a change in ChE activity resulted primarily from a shift of water into or out of the intravascular compartment. If the maximum plasma ChE activity for each case of toxemia of pregnancy, rather than the minimum value, had been used to calculate the mean enzyme activity, the activity for the toxemic group would have been actually greater than that of normal pregnancy (0.77 compared to 0.66 pH unit per hour). Such an increase in enzyme activity in toxemia of pregnancy above that of normal pregnancy is not inconsistent with the concept that the variation in plasma ChE activity in pregnancy results primarily from hemodilution, since Dieckmann has shown that relative hemoconcentration is usually present in cases of severe toxemia of pregnancy and that in such cases marked changes in plasma volume may occur within a few hours.[11]

Conclusions

1. There is a decrease in plasma ChE during the second and third trimesters of normal pregnancy to about 79 per cent of that of the nonpregnant state.

2. The degree and the time of onset of this reduction coupled with the inverse relationship demonstrated between plasma ChE activity and plasma volume within the same subject indicate that the decrease in normal pregnancy results primarily from hemodilution.

3. Plasma ChE activity in severe eclamptogenic toxemia of pregnancy was not found to be abnormally low.

4. At term maternal and fetal mean plasma ChE activities are equal.

5. By the sixth postpartum week plasma ChE activity has returned to the normal nonpregnant level.

I am grateful to Misses Helen Karlovec and Ruth Wagner and Mr. Richard Bright for their technical assistance.

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PREVENTION OF NEONATAL ASPHYXIA WITH THE USE OF A ROCKING RESUSCITATOR

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SO MUCH interest has been shown in the application of Eve's[1, 2] principle of rocking resuscitation to the prevention of asphyxia of the newborn, both in this country and abroad during the last four years, it is deemed advisable to analyze its value for this purpose by reporting the results at the North Country Community Hospital, Glen Cove, Long Island, where an automatic, electrically operated, rocking bassinet has been kept constantly available in the delivery room since it was described by Millen and Davies[3] in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY in 1946.

During these eight years two of us have performed 4,000 consecutive deliveries of infants of over thirty weeks' gestation with an uncorrected fetal loss of 34, or 8.8 per thousand, including stillborn infants, those with congenital anomalies, those that died in the neonatal period, etc.* During this series, no other form of resuscitation was used and it was felt that no child of thirty weeks' or greater gestation who had any fetal heart activity at birth was lost through the inability to provide proper ventilation.

Although references to resuscitation date back to the Bible in II Kings, Chapter 4, verse 34, where it says, "He lay upon the child and put his mouth upon his mouth, and his eyes upon his eyes and his hands upon his hands: and . . . the child waxed warm," a marked interest in resuscitation of the newborn has occurred in the last ten years as indicated by the many articles about and special apparatuses devised for this condition. This is due in a large measure to the elimination of difficult traumatic labors by the improvement in obstetrics that has preceded this decade. From this it becomes apparent that, though rare, tardy ventilation in the newborn infant is no longer a predictable matter. Furthermore, the increasing opinion that mere survival of the baby is not enough, when delays in oxygenation may cause cerebral damage, gives rise to widespread investigation of this problem.

Techniques of Resuscitation

Although there, no doubt, will always be in resuscitation of the newborn, as in any medical problem, individual preference and success with different methods, such as phrenic stimulation as advocated by Sarnoff[4] in this country

*When these figures were becoming apparent, one of us (R. S. M.) made a point of studying all of the available literature and discussing this problem personally with many American and European authorities and communicating with others by mail. One of the other authors (A. F. R.) compared the results with other methods by other doctors at our institution. The third author was working part of this time on a research fellowship in neonatal pathology.

and Kenneth Cross[5] in England and gastric oxygen as popularized by Mary Crosse[6] in Birmingham, England, a greater understanding has been obtained as obstetricians, pediatricians, anesthetists, and obstetrical pathologists have worked together and recognized certain fundamental factors common to all groups. Thus certain principles have become increasingly important. Gruenwald[7] has pointed out that the difficulty may occur (a) in utero, (b) in the delivery room, and (c) in the nursery. Karpovitch[8] has emphasized the value of regarding respiration as a diphasic mechanism in which the exhaling of carbon dioxide plays an important part. Three methods provide this: the Nielsen[9] manual method, the "iron lungs" (the one most recently described by Donald and Lord[10] can be cycled with the babies' faint efforts), and Eve's rocking method. It is obvious that the Nielsen back pressure-arm lift method might prove traumatic and requires constant attention by trained personnel. The respirators demand a great deal of attention, special equipment, and delay in being put into operation.

Eve[11] and Eve and Forsyth[12] have established the importance of improving the circulation as well as the ventilation. The efficacy of improving circulation is advocated by Smith[13] who writes that, while most normal babies start breathing because of a sensory stimulation of the skin, those with impaired respiration do so from a central nervous system stimulation. He has stated that the confluent stream from the umbilical vein and the inferior vena cava reaching the auricle consists of the most oxygenated blood coming to the heart. Until pulmonary ventilation by natural or artificial means provides for oxygenation via the pulmonary circulation, this is the most oxygenated blood in the fetus and its circulation should be stimulated. Smith also points out that the baby's own respiratory efforts at inspiration are far greater than the level above which positive pressure mechanisms to initiate respiration are dangerous. Apgar[14] and Day[15] have pointed out the frequency with which lung "blowouts" have occurred even when positive pressure machines are kept below the so-called danger pressure. Gruenwald[16] has demonstrated that when positive pressure is applied to a lung all of the alveoli do not expand equally. Certain ones dilate to the maximum before others open at all. This undoubtedly accounts for many blowouts.

Although the skilled anesthetists, now a part of every good surgical team, often use endotracheal anesthesia and positive pressure in surgery on adults, the unequal expansion of the alveoli, plus the fact that the baby's trachea is relatively small and the mucous membrane easily traumatized, has led Clifford[17] to state the hazards of tracheal intubation for aspiration or positive pressure. The Herring-Breuer[18] reflex, by distending the alveoli and, therefore, affecting the vagus nerve, will stimulate respiration. This can be done with expired air (16 per cent oxygen) as blown in the time-honored mouth-to-mouth respiration or with helium or nitrogen without any oxygen which establishes the effect as mechanical and not as due to the beneficial factor of oxygen. Certain contraindications to the routine use of positive pressure must be mentioned, however. Anderson[19] writes that the Council on Physical Therapy of the American Medical Association, in accepting the E. & J. Machine, points out that it compresses the capillaries and, therefore, impedes the blood flow, an important circulatory factor in respiration. Furthermore, positive pressure interferes with the venous return. This can be overcome to some degree if the inspiratory positive pressure phase is short and the exhalation phase is prolonged to allow for the large vessels to empty their venous return into the thoracic cavity.

Potter[20] has shown that fluid can be absorbed from the lungs, and Gruenwald[16] has pointed out that a small amount of amniotic fluid moisture in the lungs might actually change surface tension. Sanders[21] has established the

value of a rocking bed for improving circulation, which Wright[22] adopted successfully to overcome respiratory paralysis induced by poliomyelitis.

Some authors define the word "resuscitation" as an act that takes place when a being apparently dies and then is revived. Others define it as occurring only when a baby has actually never breathed, has been pronounced dead, and then has breathing initiated. An even larger group considers that any act to aid impaired respiration is one of resuscitation.

The fact that there have been cases reported of babies pronounced dead and left in the morgue only to begin crying clearly points out the difficulty in trying to prove which baby aided in respiration would not have breathed unaided. Furthermore, there are conflicting opinions as to how much anoxia a baby can stand. This unpredictability, as well as the undesirability of withholding treatment for alternate cases, makes the running of controls as desired in a true scientific study an extremely difficult one. Therefore, analogies must be made with certain adult physiologic and pathologic entities in the realization that the most frequent problem is presented by the baby in whom depressed or partial asphyxia is caused by uterine dyfunction rather than by the baby who has some inherent pathologic entity in the lungs requiring a magic form of opening the lungs. Gruenwald[7] has stated that in some premature babies lung and brain tissues have areas where the cellular development lags behind in growing away from the embryonal type of cells. It is particularly important in these babies who need respiratory assistance not to damage their limited number of functioning alveoli with positive pressure but to aid the circulatory factor and both the inspiratory and expiratory phases of ventilation.

Use of Rocking Resuscitator

Our figures are not so outstanding that one could immediately say this is the best machine to use. They are sufficiently satisfactory, however, to make us feel that we are correct in assuming we are giving the babies adequate care and attention.

In the initial use of the rocking bassinet, babies were placed in the machine upon development of cyanosis following delay in respiration and it was noticed that they became pink and free of cyanosis before they actually started to breathe satisfactorily on their own; and in some instances before they had taken even a gasp.

As time went on it became apparent that the intelligent thing to do was to place the baby in the automatic rocking resuscitator as soon as its mouth had been aspirated and the cord had been tied and severed unless the baby was breathing satisfactorily at that stage. In fact we now put all the babies in the rocker as we use it as a bassinet, but we turn on the switch and start the oxygen flowing only for the very infrequent but unpredictable baby who has not started to breathe by this time.

For an interval after the rocker was initiated as a bassinet, some of the staff physicians failed to use it until a baby had developed considerable cyanosis and had not responded to such procedures as sensory stimulation by rubbing the skin, injections of chemicals into the umbilical vein, etc. The open top enabled others to do these procedures and have the machine rocking. As they became aware that the rocking would initiate respiration they gave up the other procedures and gradually accepted the machine for its true value.

In addition to the 4,000 deliveries by two of us, a number of other infants have been presented to us by other obstetricians for resuscitation. However, during the extended period of eight years with a service of approximately 2,000 patients per year in the Hospital, there have not been a large enough number of babies who really needed resuscitation to enable us to reach

any startling conclusions. Nevertheless, such definite clinical impressions were obtained that it was decided to take colored movies to show the changes in the skin as indicative of increased oxygenation before the baby actually started to breathe. Dr. Clement Smith[23] suggested that this would suffice in lieu of oxymeter studies which are cumbersome and difficult to obtain. After many efforts with a professional photographer it became apparent that it was going to be difficult and very expensive. Therefore, an attempt was made to show the changes in the lung field of a newborn baby by taking motion pictures of fluoroscopic screenings with the baby held in the alternate positions in which it is placed when rocking is carried out. The movies of the roentgenograms clearly illustrated a marked change in both the aeration of the lung fields and the size, amounting to an increase of about the full width of one rib with the feet lowered.

Recent reports have appeared in the literature of a manually operated rocker by Pedvis, Irwin, and Philpott,[24] of one driven by oxygen by Roberts,[25] and an electric one has been described by Handley and Handley. Modifications of the original Millen, Davies rocker have been made by and proved satisfactory to Maher of North Tonawanda, New York; Finberg of Baltimore City Hospital; Scriver of Royal Victoria Hospital, Montreal, Canada; Hawk of Indianapolis; and Goodwin of Winnipeg, Manitoba, Canada. Lee[27] has reported considerable success with an intraincubator rocker in overcoming respiratory problems in the nursery. Blood oxygenation studies on the newborn to establish the efficacy of Eve's method of resuscitation have been described by Montgomery.[28]

To emphasize the unpredictability with which one may need the machine and to correct any possible misconception that it is merely to aid a baby delivered of a heavily sedated mother, the three following cases are reported.

CASE 1.—A multipara was delivered at term with pudendal block anesthesia by low forceps. She had had preliminary sedation with 1½ grains of barbiturates, when it became apparent, with the membranes ruptured, that she was going to have a fairly short multiparous labor. This labor was not unduly hard. The baby did not breathe for eight minutes during which time it was kept from being cyanotic by staying in the rocker.

CASE 2.—After twelve hours of labor, a primipara who had had 150 mg. of Demerol, 1½ grains of Seconal, and two doses of scopolamine, 1/150 and 1/300 grain, during an eight-hour period, was delivered by easy outlet forceps.. An occult prolapsed cord was detected as the forceps were being applied but this gave no difficulty in application. This baby was flaccid and was placed in the rocker as soon as the cord was clamped and its mouth freed of mucus by aspiration. During this time the tone came back in the abdominal muscles. The color never became cyanotic although it was eleven minutes before the baby breathed. It did well thereafter.

CASE 3.—Another baby was taken out of the incubator, where the hands and feet remained blue, and improved when placed in the rocker. After a short interval the baby was returned to the incubator where the cyanosis again appeared in the hands and feet. He was then placed back in the rocker and, when the color improved, was left there for approximately eight hours, after which he had a satisfactory color.

It is our impression that among the premature babies there is less incidence of delayed impaired respiration after an apparently vigorous start at birth if they are rocked for a good half hour in the delivery room before transfer to the nursery. We have been using a mixture of 65 per cent helium and 35 per cent oxygen instead of pure oxygen for these babies as well as

for some of the term babies. It has been too short a time to have any positive conclusions, but we are inclined to think this helps. This more diffusible mixture certainly has theoretical therapeutic value.

Summary

The pathologic and physiologic factors involved in the prevention of neonatal asphyxia establish Eve's principle of nontraumatic "rocking resuscitation" as the only one that aids both important components, circulation and ventilation, and stimulates both phases of the latter, inspiration and expiration.

Statistical results of 4,000 consecutive deliveries prove the efficacy of equipping every delivery room with an electrically operated bassinet and oxygen so that it may be immediately converted to a rocking resuscitator. While the usefulness is primarily for delivery rooms, rocking bassinets have a place in the nursery equipment. The need for them there, however, will be minimal, particularly by premature infants, if they are adequately rocked at delivery in spite of apparently satisfactory ventilation.

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COLD-KNIFE CONIZATION AND RESIDUAL PREINVASIVE CARCINOMA OF THE CERVIX*

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WE HAVE felt for some time that reliance on multiple cervical biopsies alone for diagnosis of cervical cancer has been one of the reasons for widespread uncertainty in determining the true nature of early cervical carcinoma. Cold-knife conization of the cervix seems adequate for diagnosis, but is definitely not proper definitive treatment as evidenced by the presence of residual carcinoma in certain postoperative uteri. The primary purpose of this report is to evaluate these impressions.

During the past five years, a study of preinvasive carcinoma of the cervix has been in progress. There is a question as to which of the so-called "preinvasive carcinomas" actually would develop into invasive carcinoma, if left untreated. Concerning this dilemma, Novak[4] in an editorial comment recently stated, "It is the pathologic rather than the clinical aspects of this lesion which have posed the chief enigma, and caused so much floundering in this field."

The recent "debate" between McKelvey[5] and Hertig and Younge,[6] with the discussions which followed, is an excellent summary of the current authoritative opinion as to the status of preinvasive carcinoma. The situation at this hospital was such that each case of preinvasive carcinoma was examined microscopically by at least two qualified pathologists (and in most cases by four or five), two gynecologists, and one or more civilian consultants in pathology. Many of the slides of doubtful cases were referred to civilian authorities on pathology for their opinion before being called preinvasive cancer by the Gynecology Tumor Board. The basic tenet that preinvasive carcinoma involves the entire depth of the mucosal epithelium with profound alterations, as adequately described by others[7-11] has been followed at this hospital. It should be assumed, therefore, that in all of these cases the diagnosis would be confirmed by the majority of pathologists elsewhere with the possible exception of those who consider glandular involvement as early invasion.[9, 10]

When Greenhill[17] visited this hospital in 1949, and was shown the result of this study in its early stages, he was particularly impressed by three things, namely, the age of the patient, the number of cases with residual preinvasive

*The opinions and/or assertions contained herein are the private ones of the writers, and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

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carcinoma in the uterine specimen, and the abnormal ratio of preinvasive cases to invasive cases. As these unusual features have been borne out through the five-year series, a word of explanation is in order.

As this clinic deals with a disproportionately large number of young women in their teens and early twenties, the average age of the patient is considerably below the age in general clinic patients. The average age of patients with preinvasive carcinoma is 32.5 years, and of patients with invasive carcinoma it is 42.9 years (Fig. 1). Both of these figures are well below the usual published averages. By the same deduction, one should see more preinvasive carcinoma smear-screening methods.

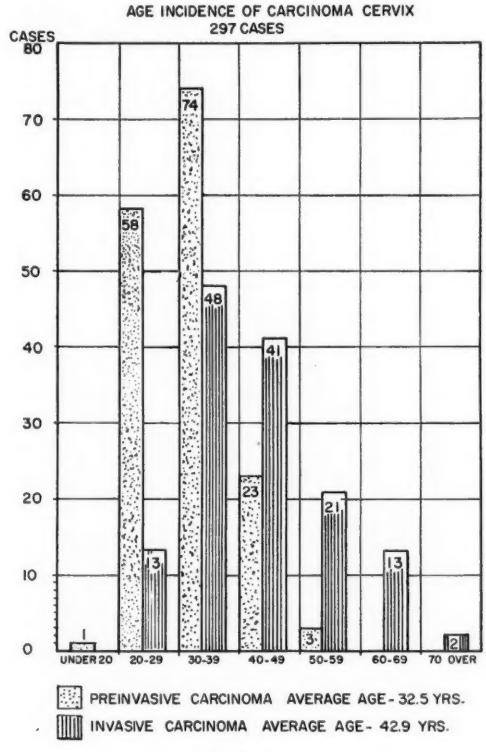

Fig. 1.

Methods

In 1949, the departments of gynecology and pathology began using the cervical smear technique of Papanicolaou and Traut[1] as a routine screening method, to detect early carcinoma of the cervix. Sarkisian[2, 3] in 1950 reported upon the first 3,420 cases examined in this manner in this clinic, with the detection of 22 cases of preinvasive carcinoma and 5 cases of invasive carcinoma. This was compared to only 5 cases of preinvasive carcinoma and 40 cases of invasive carcinoma in the six years, 1942 through 1947. With the value of the routine cervical smear thus established, it has continued to be used since that time.

Early in the study, persistent Class II and Class III smears, or single Class IV or V smears were followed by four-quadrant biopsies. At first, a Schiller iodine test was used routinely to point out suspicious areas, with no

apparent increase in the accuracy of biopsy diagnosis in a preinvasive lesion. If the biopsies demonstrated invasive carcinoma, treatment for this was begun; and in the event of negative or questionable biopsies, or a pathological report of preinvasive carcinoma, the biopsies were followed by a 360 degree cold-knife cone of the Sturmdorf magnitude. Details of diagnostic methods and treatment were reported by Baker[19] in 1949. During the first two years there was frequent disagreement between the biopsy diagnosis and the conization diagnosis; consequently, since late 1950, those "smear suspicious" cases without obvious lesions detected in this clinic have been followed by a cold-knife cone and the biopsy step has been eliminated. Up to 263 slides have been made on a single cone specimen in an effort to determine the source of the atypical cells found in the cervical smear (Table III). The perplexity for the patient, the clinician, and the pathologist has been somewhat reduced by this "short cut" to diagnosis.

The treatment for preinvasive carcinoma at this hospital has been a total wide hysterectomy, with a generous cuff of vagina, and preservation of normal ovaries. These uteri have been adequately studied, many with serial sections of the cervix, and a surprising number have shown residual preinvasive carcinoma, despite the large cone.

Cold-Knife Conization

During the five-year period from Jan. 1, 1949, to Jan. 1, 1954, 589 women were admitted to the hospital with a diagnosis of generative tract malignancy, or for conization of the cervix. In some cases these patients were referred from other hospital where biopsies and/or smears had been taken. Of these patients, 510 had conizations for treatment or diagnosis (Table I). Cones were performed in 143 cases to remove benign cervical lesions, or in conjunction with other surgery (anterior and posterior repair, etc.) for prophylaxis. The remaining 367 cones were performed to determine the presence or the absence of carcinoma of the cervix.

TABLE I. FIVE HUNDRED TEN CONIZATION CASES

For treatment of benign lesions or prophylaxis		143
No malignancies found		
Diagnostic cones		367
Malignancies found	201	
No malignancies found	166	
Total		510

Results.—In 201 of the 367 diagnostic cone cases, malignancy was found. There was no evidence of malignancy in the remaining 166 cases. Table II shows 151 cone-diagnosed malignancies in which there was no question as to the diagnosis; 91 cases were diagnosed with cone alone, and in the other 60 the cone confirmed the biopsy diagnosis of preinvasive cancer. Of primary concern in this report is the remaining group of 50 cases wherein the quadrant biopsy diagnoses created a dilemma and were misleading to the patient, clinician, and pathologist. The 18 biopsy-positive, cone-negative cases caused much concern. Others[4, 11, 13, 14, 18] have reported an incidence of from 10 to 23 per cent of such cases where only a biopsy showed preinvasive carcinoma. The doubts created in the minds of these women concerning "having cancer" or not were difficult to resolve. Consequently, 13 of the 18 had total hysterectomies, the accepted treatment for preinvasive cancer of the cervix. The remaining 5 patients without hysterectomy are being followed with no evidence of recurrence to date.

TABLE II. DIAGNOSTIC METHODS IN 297 CASES OF CERVICAL MALIGNANCY

Conization cases			201
Initial diagnosis upheld		151	
Preinvasive carcinoma on cone alone	62		
Preinvasive carcinoma on biopsy and cone	60		
Invasive carcinoma on cone alone	29		
(Note: Two cervices with preinvasive cones showed early invasion on final specimen.)			
Confusion in diagnosis		50	
Preinvasive carcinoma on biopsy; negative cone	18		
Preinvasive carcinoma on biopsy; invasive cone	15		
Negative biopsy; preinvasive carcinoma on cone	13		
Negative biopsy; invasive carcinoma on cone	3		
Biopsy inadequate; invasive carcinoma on cone	1		
Additional cervical malignancies diagnosed			96
Invasive squamous-cell carcinoma diagnosed on biopsy or fractional curettage only	85		
Invasive adenocarcinoma of cervix diagnosed on biopsy	3		
Preinvasive carcinoma on uterus specimen only (3 with negative smears; no smear on fourth)	4		
Preinvasive carcinoma on biopsy alone (residual found in uterus of each)	4		
Total cervical malignancies			297
Preinvasive cervical carcinoma	159, or 53.5%		
Invasive cervical carcinoma	138, or 46.5%		
Total	297	100.0%	

It is sufficient to state here that in 50 cases (24.8 per cent) of 201 malignancies, or 50 of the 110 cases (45.5 per cent) wherein biopsies were performed, the quadrant biopsies were misleading and resulted in a mental tumult for all concerned. By the same token, in only 2 of 201 malignancies diagnosed with cone did the uterus specimen show early invasion not found on the generous cone.

TABLE III. ONE HUNDRED SIXTY-SIX DIAGNOSTIC-CONE CASES IN WHICH NO MALIGNANCY WAS FOUND

Negative smears but suspicious-appearing cervix, or history suggestive of cervical malignancy			50
Abnormal smears			116
Cones for Class IV smears or repeated Class II and Class III smears		78	
Negative biopsy followed by still abnormal smear		38	
Cone diagnoses where smear abnormal			
Source of abnormal cells still questionable	41, or 35.5%		
Chronic cervicitis	36		
Chronic cervicitis with erosion	5		
Source of abnormal cells determined	75, or 64.5%		
Chronic cervicitis with epidermization	43		
Basilar-cell activity with chronic cervicitis	17		
Chronic cervicitis with atypical squamous metaplasia	9		
One each of:	6		
Premalignant dyskeratosis			
Premalignant cervical polyp			
Premalignant atypical epidermization			
Acute and chronic cervicitis with necrosis			
Irradiation reaction			
Endometrial hyperplasia and chronic cervicitis (smear reported suspicious for adenocarcinoma)			
	116	100%	
Total			166

In the nonmalignant group in Table III, there were 38 cases where the biopsy was apparently inadequate to rule out carcinoma. As all cervical biopsies for benign lesions have not been tabulated, this group cannot be considered statistically.

Comment.—Accurate diagnosis is of prime importance in adequate study of the nature of any lesion. Before any statistics of reasonable value can be obtained, any question as to the original diagnosis has to be reduced to an absolute minimum. Especially in the study of "preinvasive carcinoma" is conization diagnosis necessary. It has been shown that quadrant biopsies have been uncertain and misleading in 45.5 per cent of biopsy-diagnosed malignancies.

Andujar,[12] in a study of 57 selected cases of intraepithelial carcinoma, refuses to make such a diagnosis on a single biopsy specimen. Others,[15, 18] directly or indirectly, intimate reluctance to base their final conclusions on biopsy specimens and indicate their preference for circular biopsy. This study indicates that this is one of the confusing elements that can be eliminated. Conization diagnosis in this clinic has proved accurate in all but 1 per cent of the cases. The original impression that biopsy diagnosis in preinvasive carcinoma is not definite in a significant number of cases seems justified.

It is realized that many clinicians are unable routinely to cone "smear-suspicious" cervices because of the expense involved. For the same reason, neither can all cones and uterus specimens be serially sectioned. The purpose of this paper is not to advocate the elimination of quadrant biopsies in diagnosing cervical malignancy, but rather to point out the chagrin that can arise by their routine use. In order to determine, however, the true nature of the entity now being called preinvasive carcinoma, and to study accurately, follow, and evaluate statistically a large series of cases, it is felt that the biopsy-diagnosed cases should be dropped, or at least classified separately.

Residual Preinvasive Carcinoma

There are 178 cases with the initial diagnosis of preinvasive carcinoma based on biopsy and/or cone included in this study, in 159 of which the final diagnosis was preinvasive cancer. One hundred sixty-one of these 178 patients have had a total hysterectomy. Each uterus and cervix has been carefully examined for evidence of residual carcinoma and this has been found in 47 of the cases (Table IV). One hundred twenty-nine of these hysterectomies were in cone-positive cases. Residual cancer was found in 36 (29.5 per cent) of the 129 uteri, and 2 others showed early invasion.

Of the 129 conization cases which showed preinvasive carcinoma wherein the uterus was removed, 46 were qualified by the pathologist as having "extensive preinvasive carcinoma" and/or "glandular malignant metaplasia." Glandular involvement per se has not been considered early invasion in this clinic. Twenty-seven (58.7 per cent) of these were found to have residual carcinoma and three others had "premalignant" lesions in the uterine specimen. In 2 of these residual cases, early invasion was demonstrated in one section of the cervix. Both of these cases were further treated accordingly with no evidence of recurrence to date.

One death from carcinoma has occurred in this series of 159 cases diagnosed originally as preinvasive carcinoma. In this patient, 50 years of age, preinvasive carcinoma was diagnosed on a cervical cone. She had a total hysterectomy in 1951. The uterus showed residual, noninvasive carcinoma.

In August, 1952, she was thought to have cuff and parametrial involvement. A biopsy of the cuff confirmed this opinion. She was treated with radium and very radical surgery but died of complications following surgery.

This case vividly demonstrates the need for careful study of an adequate cuff specimen when treating preinvasive carcinoma with total hysterectomy. This has been stressed by Graham and Meigs.[20, 21] Hindsight analysis would suggest that preinvasive carcinoma of the vagina was present at the original operation.

Six patients in this series have had two or more conizations before definite treatment. There were 6 cases of preinvasive carcinoma of the cervical stump (3.8 per cent incidence) in this series.

TABLE IV. INCIDENCE OF RESIDUAL CARCINOMA IN 178 CASES WITH ORIGINAL DIAGNOSIS OF PREINVASIVE CARCINOMA OF THE CERVIX

BIOPSIES	COLD CONE	HYSTERECTOMY SPECIMEN	RESIDUAL PREINVASIVE CARCINOMA
No biopsy	62 preinvasive	61	19, 31.2% (1 invasive)
60 preinvasive	60 preinvasive	55	12, 21.8% (1 invasive)
18 preinvasive	18 negative	10	1, 10.0% (cone "hot")
13 negative	13 preinvasive	13	5, 38.5%
15 preinvasive	15 invasive	10 (plus irradiation)	0
No biopsy	No cone	4	4, 100%
4 preinvasive	No cone	4	4, 100%
2 called preinvasive elsewhere and nonmalignant here	2 negative	2	0

Comment.—In view of the findings of 29.5 per cent residual carcinoma in uterine specimens, we feel that conization is inadequate treatment for preinvasive carcinoma. Many times, however, because of the patient's age and desire for children, the gynecologist is reluctant to advice removal of the uterus if there is a reasonable chance for cure with less radical methods. If we assume that those who show residual carcinoma after a generous cone would develop invasive cancer, the prognosis for cure with cone alone would be 70.5 per cent. This prognosis can be analyzed better by a more complete breakdown.

The cones of the 129 cone-positive hysterectomy specimens were divided into two categories:

1. The cone diagnosis was focal preinvasive carcinoma in 83 cases. Eleven, or 13.3 per cent, of these showed residual carcinoma.

2. The cone diagnosis was extensive preinvasive cancer and/or malignant glandular metaplasia to some degree in 46 cases. Twenty-seven, or 58.7 per cent, of these showed residual carcinoma.

The cure rate in focal lesions would be 86.7 per cent; while in the extensive lesions, or those showing glandular involvement, the cure rate would be only 41.3 per cent by cone alone. This discrepancy in residual rates favors those who consider glandular involvement per se as early invasion. We have not regretted considering glandular extension as advanced preinvasive carcinoma and treating it with a wide hysterectomy.

Therefore, in advising patients as to treatment of cone-diagnosed preinvasive carcinoma, the tendency has been to consider those cases with focal

preinvasion as less hazardous. The patient in all cases makes the decision as to hysterectomy, and if such treatment is not desired all is certainly not lost with this lesion. These patients can followed with Papanicolaou smears and further conizations, if indicated, and still be successfully treated if residual or recurrent carcinoma presents itself. Accurate original diagnosis and full cooperation of the patient for follow-up are of prime importance.

Most authors agree with Hertig and Younge[6] that the only accurate way to determine what percentage of the so-called "preinvasive carcinomas" will become frank invasive carcinoma if left untreated is to make a diagnosis of preinvasive carcinoma and observe without hysterectomy or cone. As errors in diagnosis with biopsies have been shown to approximate 30 per cent of the cases of early invasive and preinvasive carcinoma, such an untreated series will be difficult to evaluate.

Residual preinvasive carcinoma in a generously coned cervix is difficult to understand except by considering preinvasive carcinoma as of multicentric origin. The excellent and meticulous study of Carson and Gall[11] with serial-block reconstructions of biopsy-positive cervices demonstrates the bizarre patterns of preinvasive carcinoma. Missing an area of epithelium with malignant change in such cases with a wide cone can be understood. Equally interesting is the impression of one of the pathologists who studied the cases in this series. He* noted areas in certain cases where the regenerated epithelium in the coned area was malignant, suggesting a physiological state of malignancy rather than a distinct lesion in the cervix.

Summary and Conclusions

1. A study of 510 conization cases and 297 cervical malignancies is presented. The use of the Papanicolaou cervical smear as a diagnostic screening method has helped detect 159 cases of preinvasive carcinoma of the cervix. The cold-knife conization as the prime diagnostic method is considered necessary for accurate diagnosis of early carcinoma. Quadrant biopsies, on the other hand, have proved difficult to interpret or misleading in 45.5 per cent of the 110 cases in which they were used.

2. The abnormal ratio of preinvasive carcinoma and invasive carcinoma (53.3 per cent and 46.5 per cent) is attributed to the young age group in this clinic. The average age of 32.5 years for preinvasive carcinoma and 42.9 years for invasive carcinoma is well below the usual published averages. The majority of the early carcinomas detected in this clinic occur in the third and early fourth decades of life. This emphasizes the need to be alert for carcinoma of the cervix at any age and not concentrate screening methods on those "over 30."

3. Residual carcinoma was found in the hysterectomy specimen of 29.5 per cent of the conization-diagnosed cases. Where the cone showed focal lesions, the residual was found in only 13.3 per cent. In those cases which showed extensive preinvasive cancer and/or some degree of glandular involvement, the residual was found in 58.7 per cent.

4. We believe that a generous conization is adequate for diagnosis but insufficient for definitive treatment in preinvasive carcinoma of the cervix.

*Robert L. Alznauer.

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HYSTERECTOMY: A COMPARISON OF THE METHODS BASED ON 2,008 CONSECUTIVE CASES

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NUMEROUS statistical studies have appeared in the literature dealing with the relative merits of the three methods of excision of the uterus (total abdominal, subtotal abdominal, and vaginal). In recent years the trend has been toward complete rather than partial removal but a number of publications indicate a divergence of opinion between two groups, one feeling that this excision should be accomplished primarily by the vaginal route,[1, 11] and the other believing that the abdominal and vaginal routes each have their specific indications and competition should not exist between them.[3, 7, 8, 10, 12] Each proponent presents excellent arguments for his choice but the bulk of these articles deal with one particular method. Few papers compare statistically two methods[2, 4] and fewer still compare three methods. Consequently, as pointed out by Leventhal and Lazarus,[4] in comparing their merits one has had to compare results from three different groups of operators, probably equal in skill but different from the point of view of heterogenous training and practice. Indeed, it would be unfair to praise or condemn the results of one method from one area by the results of the second and third methods from another area. Hence, it was decided to compare the results of the three methods by a homogeneous group of physicians, both in training and practice, to see what differences were apparent.

Material

Two thousand and eight consecutive hysterectomies were reviewed over a fifteen-year period (Jan. 1, 1937, to Jan. 1, 1952). These operations were performed on the Obstetrical and Gynecological Service of the Grace–New Haven Community Hospital, Grace Unit, by seventeen diplomates of the American Board of Obstetrics and Gynecology and the resident staff in obstetrics and gynecology.

Analysis of the 2,008 Cases

Types of Hysterectomies.—Fig. 1 shows the types of hysterectomies done and their yearly incidence. Total abdominal hysterectomy and vaginal hysterectomy imply removal of both fundus and cervix and supracervical abdominal hysterectomy implies removal of the fundus only. Twenty per cent of the operations were performed by the resident staff and slightly over one-half of all cases in the series were total abdominal hysterectomies. The group of gynecologists from whom these cases have been collected reserve vaginal hysterectomy mainly for cases of uterine prolapse, accounting for the

relative stability of the yearly incidence of this procedure. A striking shift from supracervical abdominal to total abdominal hysterectomy is demonstrated in this series, however, the transition period occurring between 1943 and 1945. This trend has been so marked that in 1951 no supracervical hysterectomy was done on the ward service and of the 7 on the private service, one was for uterine prolapse with anterior suspension of the cervical stump, 3 were section hysterectomies, and in 3 conditions were such that abdominal excision of the cervix was hazardous.

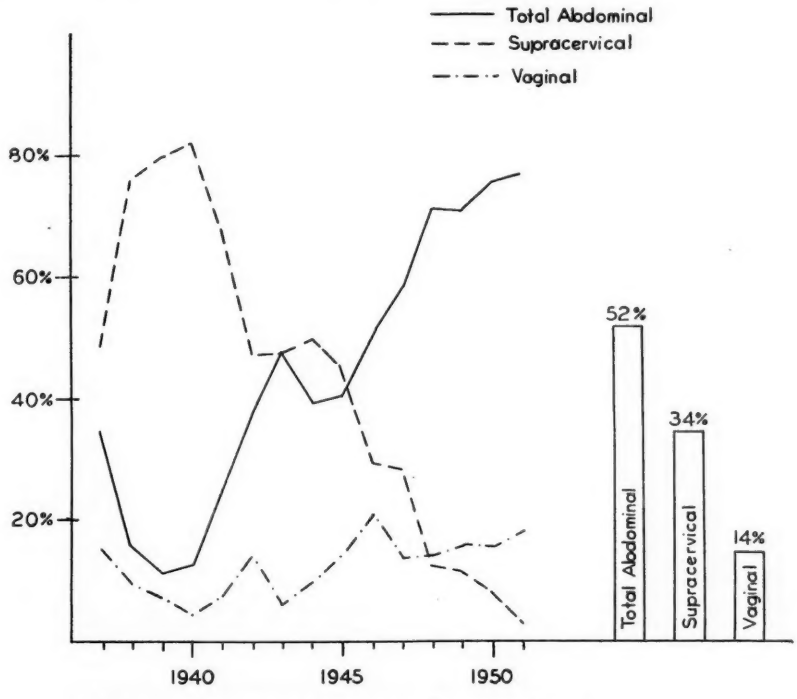

Fig. 1.—Types and yearly incidence of hysterectomies.

Age.—The average age of all patients in this series was 43.0 years. The respective average ages of the patients who had total abdominal, supracervical, and vaginal hysterectomies were 41.7, 40.3, and 54.8 years. No appreciable change was noted in the average, mean, or median age over the fifteen-year period nor was any difference noted between the ages of the private and ward patients.

Four patients were over 80 years of age and one (uterine anomaly) was 19 years of age. Of the patients over 60, the indications for hysterectomy were almost equally divided between uterine prolapse and malignancy. Hysterectomies in women under 30 years of age (119 cases, 6.3 per cent of this series) were done for pelvic inflammatory disease (55), abnormal vaginal bleeding (23), myomas of the uterus (12), complications of pregnancy (9), endometriosis (4), cervical stenosis (3), malignancy (2), prolapse of the uterus (2), uterine anomaly (1), no indication listed (2), and only on the basis of symptoms (6). Sixty-seven per cent of this group had had one or more children.

Past History.—Table I shows the past history of these patients in terms of parity, previous surgery, and relation to the menopause. ("Menopausal" is interpreted to mean that the patient is in the menopausal age group with

subjective menopausal symptoms.) The large number of multiparas and postmenopausal women in the vaginal hysterectomy group was explained previously. The 13 per cent higher incidence of nulliparas in the supracervical hysterectomy group over the total abdominal group is explained by the fact that, in the earlier years of this study when the supracervical hysterectomy was the treatment of choice, a considerable number of patients were operated upon for pelvic inflammatory disease. In the latter part of this series, as the total abdominal procedure became the treatment of choice, fewer hysterectomies were done on young nulliparas for this indication since the disease has practically ceased to exist in this area as a surgical entity.

TABLE I. PAST HISTORY

	TOTAL (%)	SUPRACERVICAL (%)	VAGINAL (%)	ALL CASES (%)
Menopausal Status.—				
Premenopausal	78.0	85.7	35.0	74.8
Menopausal	14.3	10.0	7.3	11.9
Postmenopausal	7.8	4.2	57.6	13.3
Parity.—				
Nulliparas	15.3	28.3	4.0	18.2
Multiparas	79.7	64.9	90.0	76.0
Unknown parity	4.9	6.3	5.8	5.7
Previous Surgery.—				
Patients with previous surgery	46.9	40.3	29.2	42.2
Abdominal (general surgery)	35.4	30.7	21.2	31.9
Gynecological surgery	34.6	29.4	16.4	30.2
Abdominal	19.0	17.7	6.9	16.9
Vaginal	20.8	16.2	11.7	18.0

Indications.—The indications for hysterectomy are shown in Fig. 2. These have been divided into three groups: first, those in which specific uterine pathology was present (71.8 per cent), second, those classified as the congestion-fibrosis syndrome,[9] many of which were associated with adenomyosis (15.5 per cent), and third, those in which no uterine pathology was present and the hysterectomy was done for the patient's symptoms.

The indications in the obstetrical group (27 cases) were myomas of the uterus (14), premature separation of the placenta (4), placenta accreta (3), ruptured uterus (2), postpartum hemorrhage due to uterine atony (2), cervical stenosis (1), and not listed (1). No section hysterectomy has been done for infection during the past fifteen years, the extraperitoneal section having replaced this procedure in infected patients requiring section. Hysterectomies done for therapeutic abortions (15 cases) were performed because the patient had a past history of some gynecological disorder that usually required hysterectomy, and it was felt that the procedure would be no more traumatic than hysterotomy and tubal ligation.

No indication appeared on the chart in 17 cases (0.8 per cent).

Pathology.—Only the principal forms of pathology found are discussed.

Of the 1,420 cervices removed, 64 per cent showed evidence of chronic cervicitis. The incidence of cervical epidermoid carcinoma (excluding carcinoma in situ) in these 1,420 cases was 2.6 per cent, of carcinoma in situ 1.8 per cent, and of adenocarcinoma 0.2 per cent, the average ages of these patients being 50.6 years, 45.0 years, and 37.7 years, respectively. Twenty-three of the 26 cases of carcinoma in situ were unrecognized preoperatively, the remaining 3 receiving preoperative radium therapy. Two of the 8 in-

vasive carcinomas and 2 of the 3 adenocarcinomas were unrecognized preoperatively and, of the remaining 7, all but 2 of the invasive epidermoid carcinomas received preoperative radium therapy.

The incidence of endometrial polyps was 11.9 per cent, 84 per cent of these being single.

The incidence of endometrial carcinoma was 2.8 per cent, 67 per cent occurring in multiparas and the remainder in nulliparas. Their average age was 56.7 years. The primary complaint in 70 per cent was postmenopausal bleeding, and some irregularity of vaginal bleeding was present in 96 per cent of them. Twelve cases were undiagnosed preoperatively, and 37 of the remaining 44 received preoperative intrauterine radium therapy.

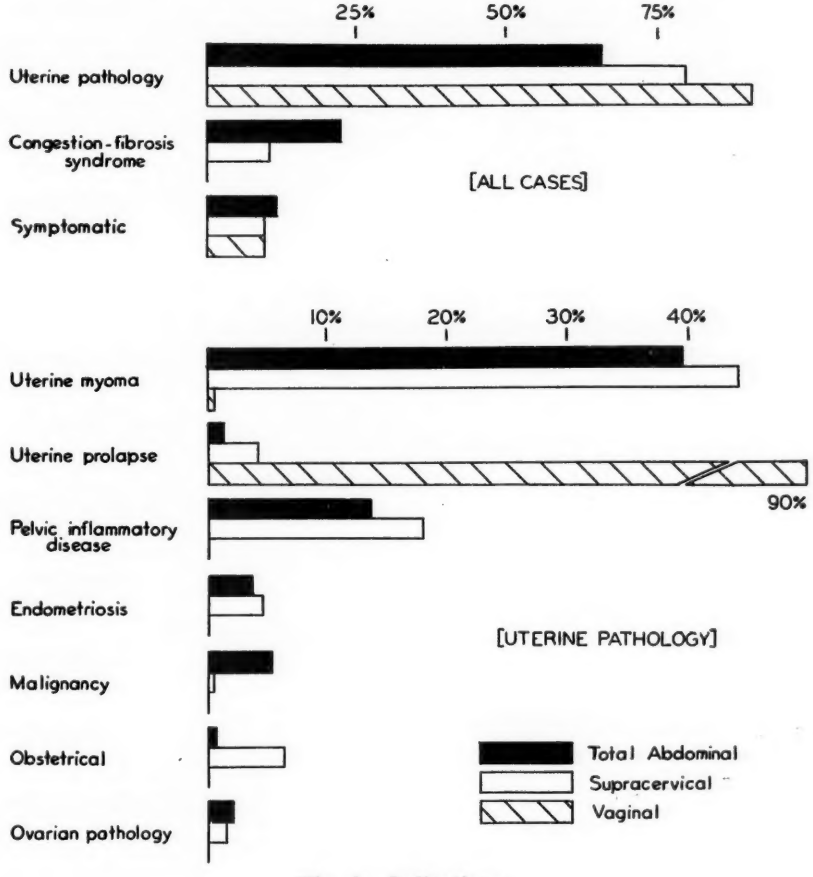

Fig. 2.—Indications.

Uterine myomas were found in 48 per cent of all uteri removed (3.6 per cent showing evidence of degeneration) and, of these, sarcoma was found in 4 cases, an incidence of 1:244, or 0.4 per cent of all myomatous uteri. Additional major fundal pathology included adenomyosis (8.1 per cent), fibrosis (9.3 per cent), benign enlargement (7.9 per cent), and chorionepithelioma (5 cases).

Functional ovarian cysts were observed in two-thirds of the cases. Nonmalignant ovarian tumors included dermoids (18), fibromas (5), serous cystadenomas (5), pseudomucinous cysts (7), Brenner-cell tumors (2), and struma ovarii (1). Of the 15 cases of primary ovarian carcinoma (0.7 per cent of

this series), 10 were adenocarcinomas, 4 were granulosa-cell tumors, and one was a granulosa-theca-cell tumor. The age of the patients with ovarian carcinoma ranged from 30 to 82 and averaged 50 years. Ten of the 15 were multiparas.

Unsuspected carcinoma (all varieties) was found in 45 cases, 2.2 per cent of this series. If cases of carcinoma in situ of the cervix, sarcoma arising in a fibroid, and fibrosarcoma of the omentum (one case) are subtracted, the total is 16 cases (0.8 per cent). These unsuspected carcinomas were endometrial (10 cases), adenocarcinoma of the cervix (2 cases), and invasive epidermoid carcinoma of the cervix ranging from early Stage I to Stage III (4 cases). The preoperative diagnosis in two-thirds of these cases was either uterine myoma or pelvic inflammatory disease.

Unsuspected intrauterine pregnancy was encountered in 12 cases (0.6 per cent), mainly varying from 4 to 12 weeks' gestation with one case of 20 weeks'. The average age of these patients was 36 years and one-half the cases were complicated by either uterine myomas or pelvic inflammatory disease.

Endometriosis was found in 3.1 per cent of the series and pelvic inflammatory disease in 12.9 per cent.

Of interest are the pathological conditions in the appendix. Three cases of appendiceal malignancy were encountered, two carcinoids and one carcinoma, producing an incidence of 1:270, or 0.4 per cent. Appendicitis was found in 6 cases, 4 of which were associated with pelvic inflammatory disease.

Anesthesia and Operating Time.—The choice of anesthesia was usually decided by the anesthetist. Inhalation anesthesia, cyclopropane (70 per cent) or nitrous oxide (23 per cent) supplemented in one-third of the cases with another agent and/or curare, was used in 85 per cent of the cases (the induction agent being Pentothal sodium in 80 per cent). Balanced anesthesia[13] has been used for the past few years. The remaining 15 per cent were given spinal anesthesia.

Slightly over 5 per cent of the operations required more than three hours to perform and almost half (49.4 per cent) were completed in less than an hour. The type of anesthesia apparently had no effect on the operating time.

TABLE II. ADDITIONAL SURGICAL PROCEDURES

	TOTAL	SUPRACERVICAL	VAGINAL	ALL CASES
Salpingectomy	679	447	11	1,137
Oophorectomy	602	356	14	972
Appendectomy	531	280		811
Perineorrhaphy	75	74	247	396
Preoperative curettage	230	119	43	392
Cervical conization	2	53		55
Cervical amputation	1	49	1	51
Cervical biopsy	35	6	5	46
Ovarian resection	18	27		45
Preoperative curettage with radium insertion	42	1		43
Extensive lysis of adhesions	20	18		38
Miscellaneous vaginal procedures	16	10	11	37
Anterior suspension of cervical stump		34		34
Cystocele repair	7	27		34
Culpocleisis			17	17
Hernia repair (ventral or inguinal)	8	6	1	15
Other	6	2	2	10

Additional Operative Procedure.—Additional surgery included any procedure done during the patient's hospital stay exclusive of the hysterectomy (Table II). Additional surgical procedures were done in 83.7 per cent of these

cases (83.5 per cent of the total abdominal, 79.3 per cent of the supracervical abdominal, and 96 per cent of the vaginal hysterectomies). The high incidence in vaginal hysterectomies is explained by the fact that almost all were accompanied by perineorrhaphy. In the group of patients who had additional surgery (1,682 cases), from one to nine procedures were performed, but only 14.7 per cent had more than four (a salpingo-oophorectomy being counted as two procedures). Bilateral oophorectomy was performed in 15 per cent of this series (12.5 per cent of the premenopausal patients, 18.5 per cent of the menopausal patients, and 27.7 per cent of the postmenopausal patients). The incidence of bilateral oophorectomy has been increasing in the abdominal procedures over the years.

Operative Complications.—In comparing the operative complications of the three types of hysterectomies (Table III), no remarkable differences were apparent. However, three factors were found to increase these complications: pelvic inflammatory disease, previous abdominal surgery, and endometriosis. The increase was most marked in the total abdominal hysterectomy group. Of the 39 cases of operative shock, 24 were primary and 11 were severe. The 15 cases of secondary shock were due to hemorrhage (12), severe anesthetic depression (2), and perforation of the uterus during curettage with the development of a massive broad ligament hematoma (1). The incidence of postoperative shock and complications in these cases was 50 and 60 per cent, respectively.

TABLE III. OPERATIVE COMPLICATIONS

	TOTAL		SUPRACERVICAL		VAGINAL		ALL CASES	
	NO.	%	NO.	%	NO.	%	NO.	%
Incidence	41	3.9	30	4.3	10	3.6	81	4.0
Shock	17	1.6	16	2.3	6	2.2	39	1.9
Hemorrhage	7	0.7	7	1.0	4	1.4	18	0.9
Bowel injury	9	0.9	6	0.9	1	0.4	16	0.8
Bladder injury	7	0.7	3	0.4	1	0.4	11	0.5
Ureteral injury	3	0.3			1	0.4	4	0.2
Other	5	0.5	5	0.7	0		10	0.5
Previous abdominal surgery*		80		17	†			49
Pelvic inflammatory disease*		146		89	‡			112§
Endometrosis*		51		†	‡			17§

*Increase in incidence of operative complications in patients with these conditions when compared to the group not having them.

†No increased incidence.

‡Not investigated.

§Based on abdominal procedures only.

Thirteen (72 per cent) of the 18 cases of operative hemorrhage were associated with shock, 7 of which were severe. Two of the cases of severe hemorrhage with shock were due to failed vaginal hysterectomy and the uterine perforation previously mentioned. Postoperative shock developed in 47 per cent of these cases of operative hemorrhage and 35 per cent of these patients became morbid.

All known bowel injuries were recognized at the time of injury and repaired. Four of the 16 patients became morbid, one of whom developed peritonitis and another pneumonia.

Of the 11 bladder injuries, 7 were recognized immediately and repaired. Two of these injuries were caused by the bladder portion of the self-retaining retractor. Two of the 7 patients with primary repairs became morbid, one of whom developed cystitis. No patient in this group developed a fistula. The

4 patients with unrecognized bladder injuries were morbid and developed vesicovaginal fistulas. The incidence of fistulas following all bladder injuries was 36.1 per cent. Two of the fistulas were successfully secondarily repaired, one healed spontaneously, and one patient refused treatment.

Of the ureteral injuries, one was questionable. It was thought at operation that it had been damaged and the patient had a postoperative course compatible with a ligated ureter. Retrograde pyelography was never done and intravenous pyelography showed a poor visualization of the kidney on the affected side. Another ureteral injury was unrecognized at time of total abdominal hysterectomy and required two attempts at closure of a ureterovaginal fistula before it was successfully accomplished. The other two injuries were questionable and identical. Each patient returned several years after total abdominal and vaginal hysterectomy, respectively, with urinary tract complaints. Intravenous pyelography in each case revealed a nonfunctioning kidney and ureteral catheterization showed a complete block within 2 to 4 cm. of the ureteral orifice. It is not known whether this was due to ligature or scar tissue contracture.

Two operative deaths occurred, one of irreversible shock produced by bleeding associated with a premature placental separation and the second due to cardiac arrest (abstracted under "mortality").

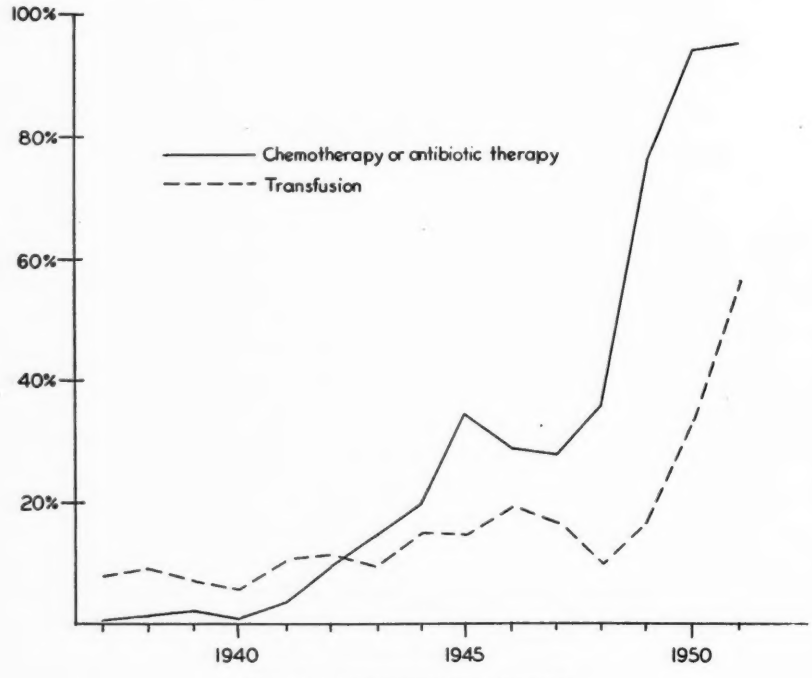

Fig. 3.—Postoperative therapy.

Postoperative Therapy.—The use of plasma for shock was limited to 9 cases during the early part of this series. From 1 to 13 pints of whole blood were given to 379 patients (18.9 per cent). The incidence of transfusions has increased steadily (Fig. 3) so that, in 1951, 55 per cent of all patients who underwent hysterectomy received at least one pint of blood. The average amount given per patient remained well under 150 c.c. until 1950 when it rose to 250 c.c., and in 1951 it averaged 400 c.c. per patient. The incidence of transfusion reactions was 4.2 per cent.

Chemotherapy and/or antibiotic therapy was used in 39 per cent of the cases, most frequently in the vaginal hysterectomy where the incidence of infectious postoperative complications was the highest. Penicillin (30.7 per cent) and sulfonamides (13.3 per cent) were given more often than streptomycin, Aureomycin, Chloromycetin, etc. (the latter in less than 2 per cent of the cases). Therapy was given for an average of 8.2 days if the 785 patients who received these drugs are considered (total abdominal, 8.2 days; supracervical, 6.7 days; and vaginal 9.0 days). If the whole series of 2,008 patients is considered, each received therapy for an average of 2.5 days. Prior to 1942, less than 15 per cent of the patients received this form of therapy. The incidence rose gradually until in 1948 35 per cent were receiving one or the other type of these drugs, and then it rose even more abruptly so that in 1950 and 1951, 94 and 95 per cent, respectively, received them.

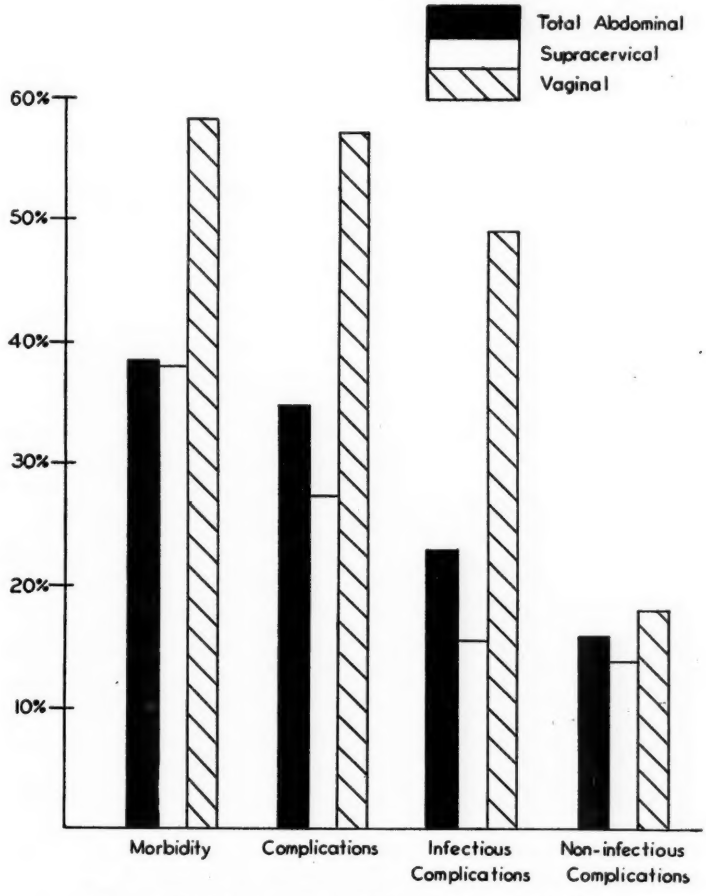

Fig. 4.—Incidence of morbidity and complications.

Voiding.—Postoperative use of retention catheters has usually been reserved for cases of known or suspected bladder injury. Consequently, 95.7 per cent of these patients were permitted to attempt spontaneous postoperative micturition but, failing this, were catheterized as needed. More than half (54.8 per cent) voided spontaneously by the end of the first postoperative day, 81 per cent of those operated upon abdominally and 51 per cent of those vaginally.

Morbidity.—For the purpose of this paper, morbidity is defined as any temperature of 100.4° F., taken orally twice daily, on any two postoperative days except the first. The incidence in all cases was 40.8 per cent, and was highest in the vaginal hysterectomy series (Fig. 4). A progressive decline in morbidity has occurred from 60 per cent in 1940 to 28 per cent in 1951. Considering all cases, 31 per cent of the patients had no days of elevated temperature, 59 per cent had one day or less, 74 per cent had two days or less, and 26 per cent had more than two days of elevated temperature. After the second postoperative day, 76 per cent of the total abdominal, 81 per cent of the supracervical, and 52 per cent of the vaginal hysterectomy patients had normal temperatures.

Half of the cases of morbidity were explained by a symptom complex and/or physical findings of a specific complication (cystitis, peritonitis, etc.). It was difficult to explain morbidity of one or two days, but as the number of days of morbidity increased the percentage of explainable temperatures increased. The "unexplainable" temperatures are given the name "operative reaction," and occurred in 51 per cent of the total abdominal, 62 per cent of the supracervical, and 29 per cent of the vaginal hysterectomy cases.

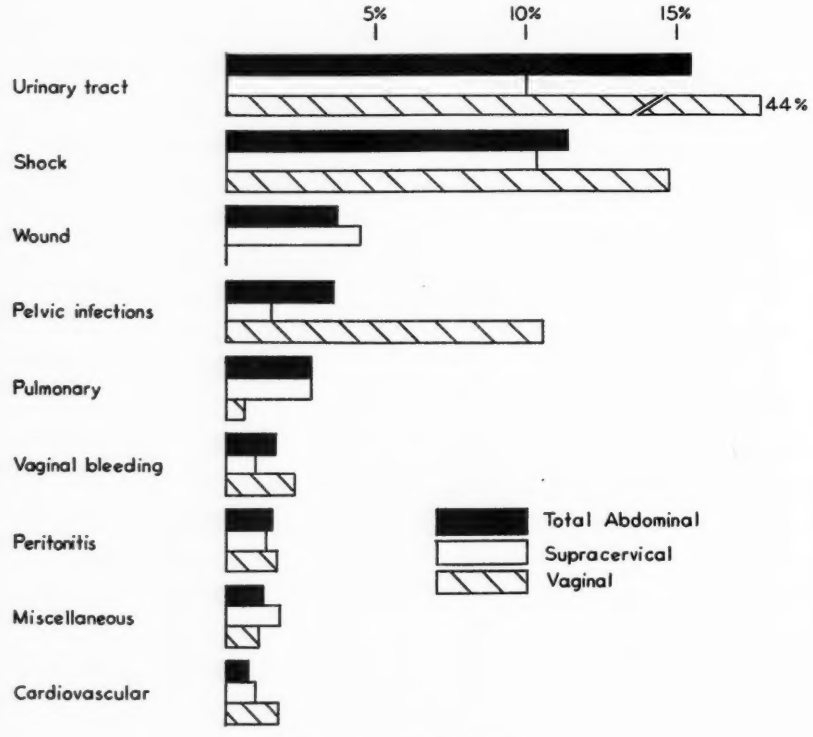

Fig. 5.—Complications.

Postoperative Complications.—Postoperative complications occurred in 34.9 per cent of the cases: 19.2 per cent infectious, 10.6 per cent noninfectious, and 5.1 per cent both (Fig. 4). The yearly incidence of complications has been decreasing, especially in the infectious group, in 1951 being 15.1 per cent (9 per cent lower than the fifteen-year average). Urinary tract complications, wound complications, peritonitis, and postoperative vaginal bleeding, as well as pelvic and pulmonary complications, have shown a steady yearly decline.

Shock has shown an explainable yearly increase. Although the morbidity of the total abdominal hysterectomy was almost equaled by that of the supracervical hysterectomy, more complications occurred in the former. Complications in the vaginal hysterectomy were high (56.9 per cent) and half of the patients (48.8 per cent) developed infectious complications. The major postoperative complications are shown in Fig. 5.

Urinary tract complications occurred in 17.5 per cent of the cases (1951: 8 per cent). They were more frequent in the total abdominal (15.5 per cent) than in the supracervical hysterectomy (10.0 per cent), and were highest in the vaginal hysterectomy (43.7 per cent). The leading complication was cystitis (16.8 per cent). An arbitrary classification of cystitis was made of mild, moderate, and severe, on the basis of laboratory findings, clinical course, and simplicity of treatment, the first two requiring the simplest of therapy. Severe cystitis occurred in 3.7 per cent of all cases: 1.9 per cent of the total abdominal, 1.0 per cent of the supracervical, and 17.1 per cent of the vaginal hysterectomies. Urinary fistulas were discussed under operative complications. Of the 4 vesicovaginal fistulas, 2 occurred in total abdominal hysterectomies, one in a supracervical hysterectomy, and one in a vaginal hysterectomy. The one ureterovaginal fistula followed a total abdominal hysterectomy.

Shock was the second leading complication, occurring in 11.4 per cent of the patients (1951: 17.5 per cent). Shock was divided into three categories: mild, moderate, and severe. Mild shock was primarily postoperative anesthetic depression rather than true clinical shock. Subtracting these cases from the total yielded a steady yearly decrease of the incidence of shock and in 1951 it occurred in two cases (1.2 per cent). Shock appeared most frequently in vaginal hysterectomy and least in supracervical hysterectomy. Secondary shock was mainly due to vaginal bleeding (1 per cent of this series) and also to severe transfusion reaction (1), evisceration (1), hemorrhagic diathesis due to anticoagulant therapy (2), and blood loss four hours after operation from a bleeding skin vessel (1).

Wound complications occurred in 4 per cent of all abdominal procedures (1951: 0.7 per cent). Of the 45 wound abscesses (2.6 per cent), 2 were secondary to hematomas and 2 required surgical incision and drainage. Three eviscerations occurred (1: 578 of abdominal procedures), all in total abdominal hysterectomies in women 44 and 45 years of age who underwent hysterectomy for pelvic inflammatory disease (1) and uterine myoma (2). These eviscerations occurred on the fifth, sixth, and ninth postoperative days and the patients were morbid, three, one, and five days, respectively.

Postoperative pelvic infections developed in 3.9 per cent of the patients (1951: 4.0 per cent), most often after the vaginal hysterectomy (10.6 per cent). Of the 33 pelvic abscesses, 82 per cent were primary and 18 per cent were secondary to an encapsulated hematoma. Ultimately 30 per cent absorbed, 45 per cent had spontaneous vaginal drainage, and 24 per cent required operative drainage (4 extraperitoneally and 4 by colpotomy). "Bladder flap infection" is defined as an infected collection of serum, blood, etc., between the vagina and bladder, the patient exhibiting a moderately febrile course that resolves when vaginal drainage occurs. The incidence of these infections was approximately that of pelvic abscesses. Of the perineorrhaphies performed, 3 per cent became infected and three-fourths of these developed abscesses.

Pulmonary complications occurred in 2.5 per cent of the patients (1951: 2.9 per cent). There was no difference in the incidence of this complication between the total and supracervical hysterectomies, but its incidence in vaginal hysterectomy was negligible. Pneumonia was found equally in the total and supracervical hysterectomy cases (in 3 instances, secondary to aspiration of

vomitus) and half as many cases were found in the vaginal hysterectomy. The difference in the incidence of atelectasis between the three types of hysterectomies was not remarkable and 2 cases were secondary to aspiration of vomitus. No pulmonary embolism occurred in the vaginal hysterectomy series and the incidence in the total and supracervical hysterectomies was almost identical (0.8 and 0.7 per cent, respectively).

Vaginal bleeding occurred in 1.6 per cent of the cases, 53 per cent requiring packing, 56 per cent showing shock, 47 per cent requiring transfusion, and one case requiring amputation of the cervical stump. Free bleeding into the abdominal cavity from a loose vessel occurred in 6 cases (1: 335—0.3 per cent); the incidence in total abdominal hysterectomy was 1:348, in supracervical hysterectomy 1:345, and in vaginal hysterectomy 1:274. No exploratory operation was performed.

Peritonitis developed in 1.5 per cent of the patients (1951: 1.2 per cent) and was equal in the three types of hysterectomies. Two cases of peritonitis were secondary to a complication involving the stump of the appendix and were also associated with a bowel obstruction. Two of the 4 bowel obstructions resolved with conservative therapy. The other two are described in the following case reports:

CASE 1.—A total abdominal hysterectomy and incidental appendectomy were performed on a 35-year-old white woman for the congestion-fibrosis syndrome. She became septic immediately after operation and an exploratory operation was performed on the fifth postoperative day. A complete obstruction of the small bowel was found at the ovarian pedicle with an abscess (*B. welchii*) around the stump of the appendix. The obstruction was relieved and a cecostomy performed. With the exception of a wound abscess, the patient made an uneventful recovery.

CASE 2.—A total abdominal hysterectomy and an incidental appendectomy were performed on a 47-year-old white woman for the congestion-fibrosis syndrome. Her postoperative course was progressively more septic and an exploratory operation was performed on the ninth postoperative day. A complete obstruction of the small bowel was found at the stump of the appendix. This was relieved and the patient made an uneventful recovery.

TABLE IV. FACTORS AFFECTING MORBIDITY AND COMPLICATIONS

	MORBIDITY			COMPLICATIONS		
	TOTAL (%)	SUPRA-CERVICAL (%)	VAGINAL (%)	TOTAL (%)	SUPRA-CERVICAL (%)	VAGINAL (%)
Multiparity over nulliparity	18	25	*	4	4	25
General anesthesia over spinal anesthesia	9	16	68	49	21	108
Additional surgery over no additional surgery	18	28	†	11	15	†
Vaginal plus abdominal surgery over abdominal surgery only	‡	43	†	21	27	†
Pelvic inflammatory disease over no pelvic inflammatory disease	54	18	†	22	‡	†
Operating time						
One to two hours over less than one hour	12	26	–14	7	58	–13
Two hours or more over one hour or less	13	72	–47	60	112	–26
Endometriosis over no endometriosis	‡	‡	†	11	‡	†

*Not valid.
†Not investigated.
‡No increased incidence.

Factors Affecting Morbidity and Complications.—A number of conditions were investigated to determine whether they were associated with an increased incidence of postoperative morbidity and complications. In this series no increase in either morbidity or complications was noted in patients who had previous surgery, uterine suspension, hypertension, preoperative use of radium, carcinoma, or who were pregnant at the time of operation. Neither the patient's age nor the season of the year affected postoperative morbidity or complications. Incidental appendectomy did not increase morbidity.

In Table IV are listed those factors which did increase morbidity and/or complications. In brief, patients who received spinal anesthesia were less prone to develop either morbidity or complications than were those who received a general anesthetic. Multiparity and endometriosis increased complications somewhat, while the presence of pelvic inflammatory disease and additional surgery, particularly vaginal surgery, increased both morbidity and complications considerably.

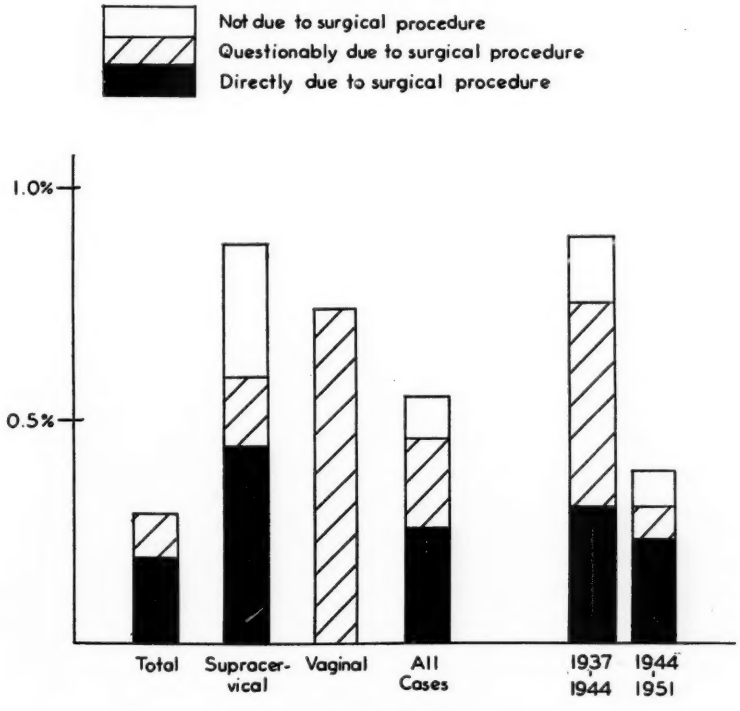

Fig. 6.—Mortality.

Mortality.—Excluding the one death from obstetrical causes following puerperal hysterectomy, the mortality rate for supracervical and vaginal hysterectomies was almost identical, 1:129 and 1:137, respectively. This was two and one-half times that for the total abdominal hysterectomy (1:348). Comparing the rates for the first and last seven and one half year periods of this series, the mortality rate was slightly more than halved, 0.89 per cent (1:112) in the former and 0.37 per cent (1:267) in the latter. The fatal cases were as follows:

CASE 1.—No. 21182, 1938. A 58-year-old white para v-v-0-0-v underwent vaginal hysterectomy for uterine prolapse. Her postoperative course was not unusual until the seventeenth day when she suddenly developed weakness, dizziness, and air hunger. The

following day her condition became worse and a precordial friction rub was heard. An electrocardiogram showed an intraventricular block and profound myocardial damage. She died of a clinical myocardial infarction.

CASE 2.—No. 23348, 1938. A 46-year-old white para x-ix-i-0-ix underwent vaginal hysterectomy for uterine prolapse. The first ten postoperative days were not remarkable but a marked asymptomatic anemia was discovered on the tenth day and the patient was given a transfusion. After receiving slightly less than 100 c.c. she developed a severe chill, a temperature of 106° F., and went into shock. She died 48 hours later markedly jaundiced, anuric, never having regained consciousness. Autopsy findings were those of a severe toxic hepatitis and nephritis due to a mismatched transfusion.

CASE 3.—No. 26688, 1939. A 30-year-old Negro para v-v-0-0-v received conservative therapy for 22 days for an acute exacerbation of a chronic pelvic inflammatory disease. No signs of active infection being present, bilateral excision of a tuboovarian abscess with involved appendix and supracervical hysterectomy were done, during which one of the masses ruptured into the peritoneal cavity. The postoperative course was septic, the patient developing a progressive generalized peritonitis with sudden death on the fifth day. Autopsy showed a large pulmonary infarct, contralateral atelectasis, and generalized peritonitis.

CASE 4.—No. 33404, 1940. A 27-year-old white para i-i-0-0-i was admitted at term, in labor, with a moderately severe toxemia and abruptio placentae. After a violent labor she was delivered by version and extraction of a stillborn child followed by the completely separated placenta. Despite oxytocics, atony persisted and the uterus was packed one hour after delivery. Two hours after delivery, with the bleeding still uncontrolled and the patient in deep shock (and still neither infused nor transfused) a supracervical hysterectomy was performed. The patient died as the procedure was completed.

CASE 5.—No. 33715, 1940. A 37-year-old white woman of unknown parity underwent supracervical hysterectomy, bilateral salpingo-oophorectomy, and appendectomy for a myomatous uterus and chronic pelvic inflammatory disease. After a normal postoperative course, she was found dead on the eighth night by the nurse on night rounds, presumably of a pulmonary embolism.

CASE 6.—No. 42141, 1941. A 42-year-old white para viii-viii-0-0-viii underwent supracervical hysterectomy and bilateral salpingo-oophorectomy for a myomatous uterus. She developed a pelvic peritonitis that cleared by the sixth day. On the eighth day, she complained of severe oppressive precordial pain with radiation down the left arm, became dyspneic, cyanotic, and died two hours after this onset of a clinical myocardial infarction.

CASE 7.—No. 66512, 1944. A 55-year-old white para v-v-0-0-v underwent supracervical hysterectomy for a myomatous uterus. She was afebrile and asymptomatic for the first 8 days, but then had a temperature of 102.4° F. and complained of dysuria. Two days later, she suddenly died of a clinical pulmonary embolism with acute dyspnea, cyanosis, and chest pain.

CASE 8.—No. 89437, 1947. A 47-year-old white para iii-ii-i-0-ii underwent total abdominal hysterectomy and appendectomy for a myomatous uterus. The patient developed a mild transfusion reaction following operation and then fulminating peritonitis. On the sixth day she received a mismatched transfusion, became completely anuric on the seventh day, and died on the eighth day with a clinical diagnosis of sepsis secondary to a generalized peritonitis and a probable lower nephron nephrosis secondary to a mismatched transfusion.

CASE 9.—No. 95067, 1948. A 61-year-old white para iii-ii-0-i-ii underwent supracervical hysterectomy and bilateral salpingo-oophorectomy for an adenocarcinoma of the fundus the size of a grapefruit involving both bladder and rectum. The patient's operative condition was poor and no further surgery was attempted. Postoperatively the patient remained free of fever and asymptomatic, but beginning on the twenty-first postoperative day she became progressively more oliguric and died in uremia on the twenty-seventh day.

CASE 10.—No. 109258, 1950. A 36-year-old white para iii-0-i-ii-0 underwent total abdominal hysterectomy for an infected incomplete abortion with a degenerating fibroid. She developed a fulminating peritonitis and died from a pulmonary embolism on the ninth day.

CASE 11.—No. 109532, 1950. A 37-year-old Negro para ii-i-0-i-i underwent total abdominal hysterectomy for a myomatous uterus under cyclopropane anesthesia. As the procedure was being completed the patient developed cardiac arrest and despite the usual measures and cardiac massage she died.

Two cases (No. 4 and No. 9) could not definitely be attributed to the procedure. The case of the puerperal hysterectomy was poorly managed (i.e., no treatment of the toxemia, traumatic delivery, two hours' delay without transfusion so that by the time the patient arrived in the operating room she was in irreversible shock). In Case 9, the patient died of uremia secondary to carcinomatous involvement of the ureters. In neither instance can the procedure be held responsible.

Four cases were questionably due to the procedure (No. 1, No. 2, No. 6, No. 11). Patients 1 and 6 died of myocardial infarction and in Case 11 death was from anesthesia rather than due to the gynecological procedure. Patient 2 died of changes secondary to a mismatched transfusion.

Of the 5 remaining cases, one might have been handled differently (No. 10: in this area, total abdominal hysterectomy is not generally considered the treatment of choice for septic abortions) and one was questionable (No. 8: although complicated by sepsis and generalized peritonitis, the patient actually died of a lower nephron nephrosis secondary to a mismatched transfusion and might have lived had not the kidneys been so badly damaged). All 5 cases, however, may be directly attributed to the surgical procedure.

Hospital Stay.—The average postoperative hospital stay was 13.4 days (12.8 days for the total abdominal, 14.2 days for the supracervical abdominal and 13.4 days for the vaginal hysterectomies). The trend has been downward, especially since 1947, until today it averages slightly less than 10 days.

Summary

A review has been made of 2,008 consecutive hysterectomies over a fifteen-year period. There has been a gradual increase in frequency of total abdominal hysterectomy (52 per cent of the entire series). The frequency of supracervical hysterectomy has consequently decreased (34 per cent of the series), while the rate for vaginal hysterectomy has remained approximately the same (14 per cent). Vaginal hysterectomy was reserved principally for treatment of uterine prolapse.

Genital malignancy occurred in 8.3 per cent of all patients; the malignancy was the indication for 6.1 per cent of the operations. Total abdominal hysterectomy has become the treatment of choice for the congestion-fibrosis syndrome in our hands, and now accounts for about 30 per cent of all hysterectomies done.

There has been little variation in age of the patients and the general indications for operation throughout the years of this study. In women under 30 years the principal indication was pelvic inflammatory disease, while in women over 30 years the indications have mainly been specific uterine pa-

thology, the most common pathological findings being myomas of the uterus (48.6 per cent) with chronic cervicitis second (64 per cent of all cervices removed).

The incidence of operative complications was approximately the same for all three types of hysterectomy. Previous abdominal surgery and pelvic inflammatory disease were found to increase operative complications considerably.

The increased use of chemotherapeutic and antibiotic agents and blood transfusions during the past few years has resulted in marked reduction in morbidity and postoperative complications. Increased morbidity and complications were observed in patients who underwent additional surgery, vaginal and abdominal procedures at the same time, where pelvic inflammatory disease was present, and, in certain instances with increased operative time. Patients who had spinal anesthesia had a smoother recovery than those who had inhalation anesthesia.

Eleven deaths occurred in this series (0.55 per cent).

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PNEUMOCOGRAPHY AS AN AID IN THE DIAGNOSIS OF GYNECOLOGIC DISEASE

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DURING the past several years, the use of pneumoperitoneum as an aid in the diagnosis of pelvic disease has received tremendous impetus largely through the influence of I. Stein and his co-workers at Michael Reese Hospital, who published their first report in 1926. Since that time, Stein has written several papers reviewing a large number of cases utilizing pneumoperitoneum for the diagnosis of gynecologic disorders.

Essentially, the procedure referred to as pneumoperitoneum or pneumocography consists of obtaining an x-ray film projected through the pelvis after the injection of gas into the peritoneal cavity. Gas is injected through the abdominal wall by needle, or through the cervix as in the Rubin test. After the injection, the patient's head is lowered, causing the intraperitoneal gas to rise and surround the pelvic organs. Thus the gas acts as a contrast medium, so that x-rays taken through the pelvis of the outlined pelvic viscera demonstrate radiographically any existing pathologic process. This type of pneumoperitoneum utilizing only gas is referred to as the "single contrast" variety. When radiopaque dye is injected into the uterus with gas in the peritoneal cavity, the x-ray thus obtained constitutes a second type, "double contrast" pneumoperitoneum.

Despite the enthusiasm of the proponents of pneumoperitoneum, it has never been widely accepted as a standard hospital procedure, probably for a number of reasons. Among the more common is the fact that the medical profession is slow to embrace a new procedure, especially if there is any element of risk involved. Second, the necessity for procuring new and possibly costly equipment has discouraged many otherwise would-be enthusiasts. Last, the time required to carry out and complete this examination has probably been considered excessive by many practitioners.

In view of the contradictory situation that exists between the advocates and the critics of this procedure, we felt that another objective evaluation of the subject was in order. In an effort to eliminate the need for special equipment (which we feel is one of the greatest barriers against its general acceptance), we have developed a technique, not previously described, which is applicable with routine x-ray equipment. At the same time, we have attempted to re-evaluate, on the basis of our experience, the indications for the use of pneumoperitoneum and the type and number of complications attending its use.

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Historical Background

Kelling, in 1902, was the first to utilize air injected into the abdominal cavity to aid in visualizing abdominal viscera by endoscopy. This procedure was not reported again until 1910, when Jacobeaus, of Stockholm, pierced the abdominal wall of 20 cadavers and demonstrated that no damage was done to the viscera by the needle. In 1912, Jacobeaus published a monograph on the subject of laparo- and thoracoscopy under air inflation. Weber, in 1912, devised a technique which utilized pneumoperitoneum to outline abdominal tumors radiographically. He conducted experiments on animals and cadavers to confirm his views, using either air or oxygen as the gas. That same year, Lorey independently made similar observations concerning the diagnostic value of intra-abdominal pneumoperitoneum. In 1914, Rautenberg used air intraperitoneally to aid in the diagnosis of diseases of the liver roentgenographically. That same year, Meyer-Betz emphasized the value of pneumoperitoneum when used to evaluate abdominal pathology, especially of the liver. In 1918, Goetze, and again in 1919, A. Schmidt reported similar observations. Orndoff, in 1919, proposed the use of oxygen and nitrogen instead of air, claiming better results with these gases.

The first use of pneumoperitoneum to reveal gynecologic disorders radiographically was made by A. Stein and Stewart in a detailed report in 1919. This work was re-emphasized by Orndoff in 1920. Stewart and A. Stein also noted, in 1919, that pneumoperitoneum in conjunction with a barium meal was much more informative than the barium meal alone in diagnosing gastrointestinal pathology. Carbon dioxide was first utilized as the intraperitoneal gas by Alvarez, in 1920, and has been practically the only medium employed since that time. He pointed out that its rapid rate of absorption was advantageous to the patient and that carbon dioxide was just as effective as oxygen or nitrogen for diagnostic purposes. Ballard, in 1920, demonstrated adhesions of the intestine to the abdominal wall using pneumoperitoneum. In 1921, Peterson and van Zwaluwenberg described a definite technique for visualizing the pelvic organs by pneumocography. They emphasized that positioning the patient was most important, and accomplished this by attaching a step-like apparatus which contained the film, to an ordinary table. The sterility of the technique was also proved by Peterson who demonstrated by culture that the gas was sterile upon aspiration from the peritoneal cavity after the initial injection. Both Rubin and Peterson proposed the use of the Rubin apparatus for introducing the gas into the peritoneal cavity via the uterus and tubes, if this route seemed advisable. Also in 1921, Peterson suggested using pelvic pneumoperitoneum as a means of diagnosing early pregnancy. This was never accepted.

In 1921, Sante described the use of pneumoperitoneum as an aid in diagnosing retroperitoneal masses. Sante and Carelli continued to do a great deal of work with pneumoperitoneum but limited their efforts to the abdominal rather than the pelvic organs. Case, in 1921, reviewed the preceding three years of pneumoperitoneum and disclosed three deaths as a result of the procedure. He attributed all three to extremely poor technique. The deaths were considered preventable. Rubin described in detail a visual flow-meter-manometer* apparatus which assured the intraperitoneal introduction of known amounts of carbon dioxide under safe pressure. This apparatus with but little modification is still in use.

Peterson, in 1922, discussed the value of pneumoperitoneum in obstetrics and gynecology. He reported 138 cases in which the preoperative x-ray diagnoses were compared with the postoperative anatomic findings. He concluded

*Made by Wallace and Tierman, 349 Broadway, New York City.

that pneumoperitoneum is of considerable diagnostic value. Yung, in 1923, observed that the normal pelvic status of a patient could be easily demonstrated by pneumocography. He suggested that by prior use of pneumocography in diagnostic problems, many exploratory laparotomies could be avoided.

Since 1926, most of the literature pertaining to pneumoperitoneum has been written by I. Stein and his co-workers. In 1926, he reported 150 cases using this procedure, and in 1931, he reported an additional 530 cases. Since then, he has written numerous articles with documentary case reports. He has also noted many modifications of his original technique and equipment. In 1928, I. Stein and Arens described a new self-retaining instrument which could be used for the Rubin test, instillation of radiopaque solution into the uterus, or transuterine pneumoperitoneum. A special x-ray table was first described in 1929 by these workers and has been successfully used in their clinic up to the present time. A more complicated modernized modification of this table was described in 1952. Much of the work concerning the "Stein-Leventhal syndrome" revolves about the use of pneumoperitoneum as a diagnostic aid in demonstrating the polycystic ovaries.

In 1944, Maxfield and McIlwain reviewed the diagnostic value of pneumoperitoneum. They concluded that "pneumoperitoneum is a valuable diagnostic procedure to be used in conjunction with other methods of examinations." In 1951, Maxfield re-emphasized the importance of pneumocography in the diagnosis of pelvic pathology and suggested that the procedure should gain widespread acceptance.

In 1946, Decker proposed the insertion of a trochar into the cul-de-sac as another route of introducing the carbon dioxide intraperitoneally. He suggested that this was the safest method available for producing pneumoperitoneum. In 1946, Lewis reported a simplified apparatus for the induction of artificial pneumoperitoneum. This method utilized two water containers. The amount and rate of instillation of the carbon dioxide are determined by water displacement.

Recently, Kunstadter, Guterman, and Tulsky suggested the use of a modified technique of pneumocography in children as an aid in the diagnosis of sex endocrine disturbances. In many cases they found it invaluable, and in not a few instances pneumocography was so conclusive that it saved the child from exploratory laparotomy. They feel that pneumoperitoneum is especially valuable in these cases because of the difficulty of doing an adequate pelvic examination on a child.

Clinical Material and Method of Study

All patients subjected to diagnostic pneumocography were on the gynecologic service of the St. Louis City Hospital during the year 1951. All were white and ranged from 17 to 60 years of age and were awaiting pelvic surgery for various indications which included uterine and/or adnexal tumors, ectopic pregnancy, and cystic ovaries. The only patients eliminated from this study were those in whom it was felt preoperatively that the procedure was contraindicated for one or more of several factors. These contraindications, as outlined by Stein, fall into two groups:

A. Contraindications to "single contrast" pneumoperitoneum: (1) excessive age, and/or poor cardiac status; (2) the presence of acute or subacute pelvic inflammatory disease; (3) a pelvic tumor or mass completely filling the pelvis. (If carbon dioxide cannot surround the mass, it cannot be radiographically outlined.)

B. Contraindications to "double contrast" pneumoperitoneum include all the conditions noted for single contrast pneumoperitoneum, as well as any

situation that would rule out intrauterine manipulation such as: (1) intrauterine pregnancy, (2) uterine bleeding, (3) purulent cervical discharge, (4) malignancy of the uterus and tubes.

Using these criteria for selection, the remaining patients were subjected to either single or double contrast pneumoperitoneum preoperatively. From these pneumograms, an attempt was made to prognosticate the pelvic findings at the time of surgery. The preoperative diagnosis as determined by x-ray was compared with the actual findings as determined at laparotomy. In this manner, the x-ray diagnosis was rated in each case in what may be referred to as "percentage of efficiency." Where there was absolute correlation, the "percentage of efficiency" was 100 per cent. Where there was correlation in three out of four of the pathologic findings, this percentage was 75 per cent, and ratings were thus determined in each case.

Equipment

The x-ray machine and table utilized necessitated no special equipment. The regular roentgenographic table that may be electrically positioned from the horizontal to the vertical was used with shoulder braces applied to prevent the patient from slipping. This simple apparatus is in direct contrast to the special tables described by Peterson and I. Stein. The table used by Peterson had steplike projections which contained the film and which were used for positioning the patient, as well as keeping her stationary while on an inclined plane.

I. Stein first described his special table in 1929. It is divided into two sections or leaves of approximately equal size. The portion that does not contain the Bucky apparatus may be maneuvered from the horizontal to the vertical. Thus a patient may be so positioned that her head and shoulders are lowered, while the hips and lower extremities remain stationary. In this manner, the patient is placed in a modified knee-chest position, which Stein believes is best for obtaining informative pneumographs.

In this series, when a double contrast pneumoperitoneum was desired, the Hudgins cannula, rather than the Rubin apparatus, was used as a means of injecting the dye into the uterus. The Hudgins cannula is a cone-shaped instrument containing a ball-valve mechanism. This cannula is "screwed" into the cervix. Radiopaque substance is injected through the core of the cannula into the uterus, backflow being prevented by the ball valve. The Hudgins cannula may be inserted into the cervix before the patient goes to x-ray, and consequently minimizes manipulation during the actual administration of the pneumoperitoneum. The majority of the double contrast pneumographs were accomplished with the use of water-soluble radiopaque preparations rather than the usual iodized oil. This was to prevent untoward reactions such as have been recently ascribed to the intrauterine instillation of Lipiodol.

The volumometer and manometer used in this series were described by Rubin in 1921. Any method of injecting carbon dioxide, which prevents excessive pressure (over 100 mm. mercury) and which demonstrates the amount of gas used, is satisfactory.

The needle used for the transabdominal puncture is the regular 3 inch No. 18 spinal needle with stylet. The needle is attached to the source of carbon dioxide by rubber tubing and an adapter.

Preparation of the Patient and Technique of the Procedure

In any diagnostic procedure such as this, it is best to explain to the patient what is to be done, and approximately what may be anticipated. All of the patients in this series were hospitalized. Hospitalization of the patient is

preferable, but with the prevailing shortage of hospital beds, this is no longer practicable. At Michael Reese Hospital, a large series of examinations has been done on ambulatory patients.

The patient should have a cleansing enema about an hour before going to x-ray. Soon after expelling this, she receives 10 mg. of morphine and 0.4 mg. of scopolamine. If the examination is to be done on an outpatient or as an office procedure, she is instructed to take the enema at home, and a grain of codeine usually suffices as premedication. It is important that the bladder be emptied by catheterization just before the gas is injected, because a full bladder clouds the roentgenographic findings and may extend into the injection field. If the procedure is to be of the double contrast type, the Hudgins cannula is inserted into the cervix before the patient goes to x-ray or while she is on the x-ray table. It should be noted that the Hudgins cannula works more effectively if the uterus is first sounded and the cervix is wiped clean of mucus.

For uniformity we used only the transabdominal route. Pneumoperitoneum is accomplished in the following manner. With the equipment for transabdominal injection ready, the patient is placed on her back on the x-ray table. The skin is infiltrated with Novocain about one inch to the left of and below the umbilicus. The spinal needle with its stylet is inserted through this infiltrated area. After the skin is pierced the first resistance is encountered in passing through the fascia. Beyond this, the peritoneum is indicated by slight momentary pain on the part of the patient. The stylet is then removed from the needle and the carbon dioxide apparatus attached by means of its adapter. About 800 to 1,000 c.c. of the gas is injected rapidly into the peritoneal cavity. The needle is then removed. If double contrast pneumoperitoneum is to be done, the radiopaque substance is injected into the cervix through the Hudgins cannula at this time. The patient is then turned over onto her abdomen and, with the shoulder braces in place, the head of the table is lowered to an angle of 40 degrees with the horizontal. The patient's abdomen is then "jiggled" to enable the gut to fall out of the pelvis. The intraperitoneal gas is thus allowed to rise and surround the pelvic viscera.

To determine the best position of the x-ray source, three roentgenograms were taken routinely. The first was with the x-ray source perpendicular to the floor, the x-rays striking the film at an angle of about 50 degrees. The second roentgenogram was taken with the source perpendicular to the x-ray table. The third was taken with the x-ray source placed midway between the previous two, or at an angle of 25 degrees to the table and film. In all cases, the source was 32 inches from the center of the film.

Results

Transabdominal pneumoperitoneum was carried out in 161 instances. In 3 patients, the carbon dioxide was injected extraperitoneally. Unsatisfactory films were obtained in another 5 patients because of previous extensive abdominal surgery which made it impossible to insert the needle into the abdominal cavity. In 108 of the remaining 153 cases, pelvic surgery was performed following the procedure, and in these the x-ray interpretations were correlated with the actual pelvic findings.

There is no need to list the pre- and postoperative diagnoses, which would be lengthy and uninformative. Suffice it to say that, in our hands, we considered the procedure to have on the average an "efficiency" of approximately 75 to 80 per cent. In many instances there was 100 per cent correlation. The lowest "percentage of efficiency" was 50.

Fig. 1. Fig. 2. Fig. 3.

Fig 1.—Pneumograph taken with the x-ray source perpendicular to floor. Note the marked distortion of the size of the pelvic organs. Compare with Figs. 2 and 3, taken at the same time on the same patient.

Fig. 2.—Pneumograph taken with the x-ray source perpendicular to the table. There is no distortion but the pneumograph is relatively uninformative.

Fig. 3.—Pneumograph taken with the source at an angle of 25 degrees to the table. There is minimal distortion. The findings of a normal pneumoperitoneum are demonstrated: *a*, body of uterus, *b*, fundus of uterus, *c*, ovaries, *d*, bladder, *e*, round ligament, *f*, adhesions of gut to left adnexa.

The x-ray department used various dosages and voltages, and were of the opinion that the best results were obtained by the use of the usual gall-bladder technique.

It has already been noted that three pictures were taken in each case, the only variation being in the source, as the table and patient were constantly at an angle of 40 degrees. The differences in these pneumographs are shown in Figs. 1 to 3. Fig. 1 shows an essentially normal pneumoperitoneum taken with the x-ray source perpendicular to the floor. Note the marked distortion of the size of the pelvic organs resulting from the acute angle at which the x-rays strike the film. The roentgenogram in Fig. 2 is of the same patient, taken at the same time, except that the x-ray source is now perpendicular to the table and film. There is no distortion, but the bony structures of the pelvis partially mask the outline of the pelvic organs. This often results in unsatisfactory roentgenograms. The pneumograph shown in Fig. 3 demonstrates the third technique, and proved to be the most informative film. It represents a compromise between the techniques demonstrated in Figs. 1 and 2. The x-ray source in this case is at an angle of 25 degrees to the table and the film. There is distortion, but it is minimal, and is considered in interpreting the films. Familiarity with this distortion renders it of little consequence. Also, with this technique, the bones of the pelvis do not interfere with the interpretation of the pelvic status. Fig. 3 also demonstrates the findings of a normal pneumoperitoneum. The body of the uterus (*a*), the fundus of the uterus (*b*), the ovaries (*c*), the bladder (*d*), the round ligament (*e*), and adhesions of gut to the left adnexa (*f*) are all easily seen.

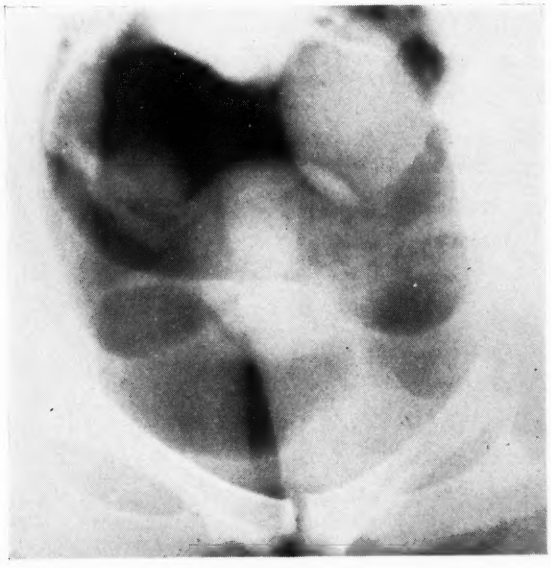

Fig. 4.—Pneumoperitoneum demonstrating an ovarian cyst measuring 8 cm. in diameter.

An example of how vividly an ovarian cyst may be demonstrated by pneumoperitoneum is shown in Fig. 4. This simple cyst of the ovary was estimated to be 8 cm. in diameter by x-ray and proved to be 7 by actual measurement. Note that, in this case, the pelvis is free of adhesions, and that this condition can be diagnosed by such a film.

A right ectopic pregnancy is shown in Fig. 5. The irregular outline of the mass, plus its increased density would lead one to suspect such a diagnosis, especially if the history is consistent. A tuboovarian mass on the basis of in-

fection would seem unlikely in the absence of adhesions. This diagnosis of ectopic pregnancy was confirmed at laparotomy, the mass measuring 8 cm. in diameter.

Fig. 5.—Pneumoperitoneum of a right ectopic pregnancy, indicated by a rather dense irregularly shaped adnexal mass.

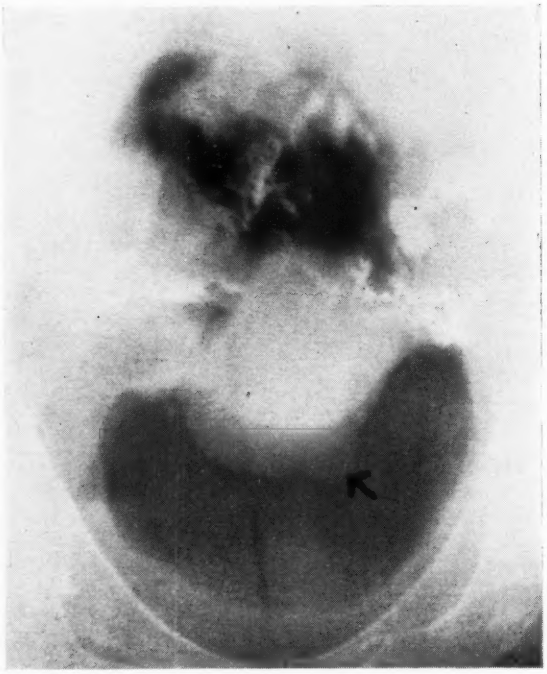

Fig. 6.—Pneumoperitoneum showing that subserous fibroids may be easily demonstrated radiographically.

Subserous fibroids may be easily demonstrated as is shown in Fig. 6. In this case, nodules could not be palpated on bimanual examination because of the obesity of the patient. Note the radiopaque material in the gut from a previous barium enema.

There were no serious complications encountered in this series of 161 cases. This agrees with the reports of Stein and other writers who have never had a death as a result of administering a pelvic pneumoperitoneum. We had no case of peritonitis following this diagnostic procedure, although cases have been reported of an occasional flare-up of an old inflammatory disease. No complications were experienced with the use of water-soluble radiopaque material for double contrast pneumoperitoneum.

Usually, a certain amount of discomfort is noted by the patient during the procedure. In our experience, we found that 75 per cent of the patients complained of pain, and that 5 per cent were extremely uncomfortable because of associated nausea and vomiting, as well as abdominal and shoulder pain. The following day, each patient was questioned about her subjective reactions to the procedure. Ninety-seven per cent felt that the procedure was tolerable. The others claimed they would have refused it had they known what it was like. Residual shoulder pain seldom lasted over six to eight hours. It should be noted that, because of the sedation given the patients in this series of cases, about 20 per cent of them did not remember going to x-ray, although they may have had discomfort at the time of the procedure.

Comment

The diagnostic procedure of pneumoperitoneum adequately demonstrates pelvic disease. It is especially effective for ovarian cysts, adnexal tumors, and subserous fibroids. Tuboovarian masses secondary to pelvic inflammatory disease can seldom be adequately visualized by pneumocography, for these are usually bound down to the surrounding structures and cannot be outlined by the carbon dioxide. By the same token, tumors filling the pelvis cannot be demonstrated. In such cases, pneumocography is unnecessary for diagnosis.

Of primary importance, one must realize that pneumoperitoneum has its limitations as well as its indications. When utilized correctly, there is no question of its merits as an adjunct in the diagnosis of pelvic disorders. In the stout or the noncooperative patient, the pelvic organs may be radiographically outlined, when a bimanual examination will be relatively uninformative. On several occasions, patients presented themselves with pelvic pain, and various examiners could not agree upon their abdominal and bimanual findings. In most cases, pneumoperitoneum demonstrates, beyond a doubt, the presence or absence of a lesion. In several instances of acute abdominal pain in which the patient did not know the extent of earlier pelvic surgery, we were able to determine accurately what had or had not been removed previously. Such information is invaluable. There were 3 cases where the uterus was thought to be fibromyomatous, but a normal pelvis was demonstrated conclusively by pneumoperitoneum, thereby saving the patient an operation.

As has been noted, adhesions between the gut and pelvic organs are easily demonstrated. This may be of benefit when patients are evaluated preopera-

tively to determine by what route the uterus should be removed. Many operators feel that, should adhesions be present, the abdominal approach is to be preferred.

We strongly believe that teaching institutions should include in their gynecologic training program the essentials of pneumoperitoneum, and should familiarize the residents with an acceptable technique of performing this type of examination. Each graduate should know how to use pneumocography as a diagnostic procedure, realizing its indications and limitations.

Most important, there is no need to submit a patient to this procedure if the examiner knows the extent of the pelvic disease. One is not justified in subjecting a patient to discomfort to verify disease that he already knows exists. In the majority of cases, diagnosis is easy and bimanual examination in itself is quite adequate. We feel that if the procedure is not used indiscriminately it will not fall into disrepute. It must be remembered that pneumoperitoneum is not a panacea as a diagnostic procedure, and it is not infallible. Its limitations must be appreciated. At best, it is only an adjunct in the diagnosis of gynecologic disorders but, as an adjunct, it is extremely valuable.

Summary

1. One hundred and sixty-one cases of transabdominal pneumoperitoneum are evaluated.

2. An acceptable technique for administering pneumoperitoneum without the aid of special equipment is described.

3. The Hudgins cannula is introduced for use in the double contrast type of pneumoperitoneum.

4. The indications and contraindications to pneumoperitoneum as a diagnostic procedure are discussed.

5. The complications of administering this diagnostic procedure are noted, and that pneumoperitoneum is a safe procedure is emphasized.

6. The limitations of pneumoperitoneum are outlined, with emphasis on the utilization of this procedure only when indicated, as an aid in diagnosis.

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Department of Case Reports
New Instruments, Etc.

AN INSTRUMENT FOR SELF-EXAMINATION OF THE CERVIX

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ALL too frequently, physicians, in the course of routine pelvic examinations, encounter gross pathological lesions of the cervix which have existed for some time entirely without the patient's knowledge. It is extremely unfortunate that such a common site of often fatal cancer is obscured from the patient's view by only a few inches of collapsed vaginal wall. If it were possible for a woman to inspect her own cervix at monthly intervals, abnormalities could be reported to physicians earlier. Skin and mouth cancers are reported earlier because they can be easily seen.

The few inches of collapsed vaginal wall obscuring the cervix from view should not be considered an insurmountable barrier, particularly when the rewards for persistence in attempts at seeing the cervix may be great.

The instrument described in this paper and shown in Fig. 1 is the result of considerable experimentation with several models. The present instrument is simply constructed and can be manufactured economically. It consists essentially of two components: (a) The rod for insertion into the vagina and (b) the mirror which is attached to the end of the rod by two small plastic arms. The rod itself is of solid clear lucite. It is one inch in diameter and seven and one-half inches long. The vaginal end has slightly rounded edges for easy insertion and has been cut at a 25 degree angle so that the surface will be parallel to the cervix. The end which remains outside the vagina is cut at right angles to the axis of the rod. Both surfaces are highly polished and, as a result, the vaginal rod is perfectly transparent. The mirror is 1¼ inches in diameter and is slightly concave. It is attached to the lucite rod 2 inches from the end by two small lucite arms. The mirror is attached in such a way that its angle of reflection can be changed through 360 degrees. The mirror itself is housed in a fitted lucite covering which protects the silvering. A small picture in color of a normal cervix, enclosed and protected by plastic, is attached to the back of the mirror. The concave mirror increases the size of the cervical image about 50 per cent.

The instrument has a clean appearance and is easily cleaned with soap and water or mild antiseptic. The fact that a solid rod is used has many advantages. The solid lucite has the property of being able to pick up external light and direct it along the axis of the rod. This solves an important step in developing any instrument for seeing the cervix, namely, a good light shining on the cervix without any attached illuminating devices. The solid rod is more easily cleaned than a tube. The solid rod also will prevent any possible self-treatment or medication by the patient. The lucite rod being perfectly

smooth and well polished can be easily inserted by the patient with no danger of injury to the vaginal mucous membrane. The rod has no crevices or joints which might be hard to clean.

The physician should demonstrate the instrument and instruct the patient in its use. The patient is cautioned against self-diagnosis and should be urged to report any changes in the appearance of the cervix just as she would request medical advice after noticing any unusual blemish or lesion on any other area of the body.

A woman who has a marital introitus should be able to use the instrument. A good time for its use and a time that will result in regularity of use is the period immediately following menstruation in women under the menopausal age. It is hoped that the establishment of such a habit will ensure its continued use at monthly intervals after the menopause.

The patient should first empty the bowel and bladder and should take a cleansing douche before attempting to use the instrument. The lithotomy position with legs widely separated relaxes the perineal muscles and will allow the instrument to be introduced easily. A clear surgical lubricating jelly is used sparingly along the outside surface of the instrument. The patient separates the labia with her left thumb and forefinger and gently inserts the rod into the vagina at a first horizontal and later 45 degree angle with the body. The rod itself may be rotated on its own axis to accommodate the inner surface of the instrument to the cervix which may be pointing either posteriorly or along the vaginal axis. A flashlight or ordinary light bulb is used for illumination. The light is directed so that the rays fall on the outside surface of the rod. The patient then sees the cervix by adjusting the mirror. The ease of seeing the cervix will increase with continued use.

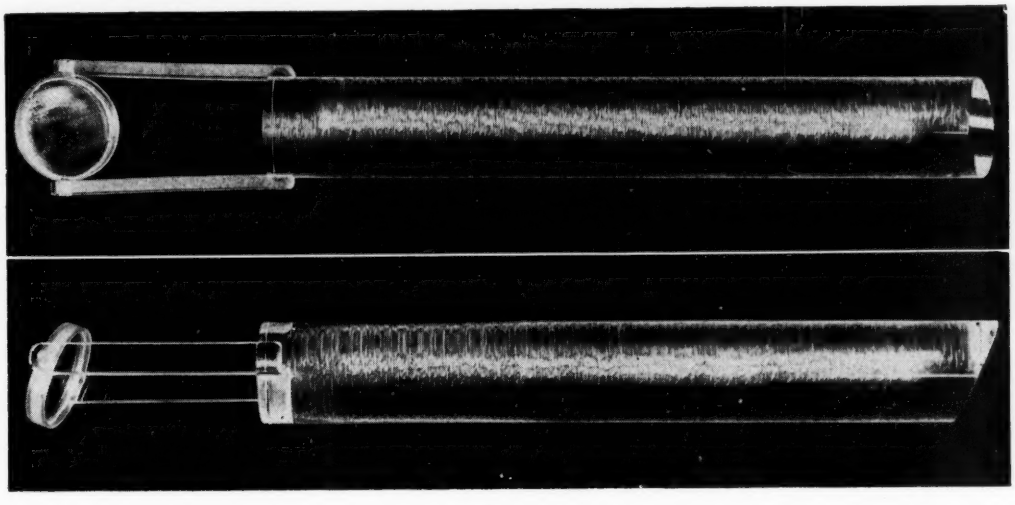

Fig. 1.

Some physicians may fear that the patient will become unduly concerned about her anatomy and thereby develop neuroses. This, of course, is possible. Everyone realizes, however, how very difficult it is to describe to the patient variations in the cervix requiring diagnosis or treatment. An accurate visual knowledge of cervical lesions should help to dispel fear.

Undoubtedly, difficulty will be encountered in teaching some patients to use the instrument; possibly there will be some physicians or lay persons who will find reason to obstruct progress along the lines of inspection of the cervix as outlined in this paper. It must be remembered, however, that our reward

for overcoming these obstructions may be very great. If only a few patients' lives could be saved by utilizing this method for early detection of cervical cancer, it would be worth while. If we could observe the lining of the stomach by as easy a method, it would be utilized by all thinking persons. Yet the cervix is a much more common site of cancer than is the stomach.

The possibility of curing or arresting cervical cancer is much greater in early lesions. In spite of this, many patients first report to their physicians for treatment with large growths that must have existed and could have been visually detected many months or even years earlier.

For these reasons we must not stop in our efforts to provide a satisfactory method for self-examination of the cervix. If this instrument is not adequate, then other instruments and methods must be developed. Our reward for eventual success will be great. The women who utilize this method have nothing to lose and much to gain.

It is hoped that many physicians and clinics will further this method of cancer detection. The way has been paved by the fine work done in self-examination of the breasts.

A slightly larger model of the same instrument has also been developed and can be used by every physician in his office to demonstrate the cervix to the patient. This model will enable the physician to show normal as well as abnormal conditions.

I wish to thank Mr. Calvin R. Menchen of the radiation branch of the National Cancer Institute for his invaluable help in constructing this instrument.

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HYPERINSULINISM AND PREMENSTRUAL TENSION: REPORT OF A CASE OF HYPERPLASIA OF THE ISLETS OF LANGERHANS

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THE association of hypoglycemia in normal women with the symptoms of premenstrual tension has been pointed out by Morton.[7] Symptoms of hyperinsulinism due to islet-cell adenomas of the pancreas have been noted to have a direct relationship to the menstrual cycle.[2, 10] Hyperplasia of the islets of Langerhans as a cause of clinically severe hyperinsulinism and hypoglycemia is relatively uncommon. In a review of 398 cases of islet-cell adenomas of the pancreas, Howard and associates[3] included 81 additional cases of hypoglycemia in which no pancreatic tumor was found on exploration or subsequently. Of these, hyperplasia of the islets of Langerhans was reported in 18 instances, and a cure effected by subtotal resection in 10. Four of the patients were adult women; the relation of symptoms to their menses was noted in two instances,[5] in one the symptoms being observed "particularly just preceding or just following menses"; in the other, "increased in frequency at the time of menses."

The following case of hyperinsulinism associated with hyperplasia of the islets of Langerhans is presented to emphasize the influence of the menstrual cycle on the symptoms of hypoglycemia.

Case Report

Mrs. E. C., a 43-year-old Italian housewife, was admitted to Mercer Hospital on April 15, 1954, complaining of attacks of weakness, dizziness, faintness, numbness and tingling of fingers and lips, sweating and nervousness of sixteen months' duration. These attacks occurred chiefly in the morning before arising, and could be relieved by taking "something sweet." The patient stated she felt as if her mind were a "blank" on these occasions. Other attacks occurred in the afternoon when her stomach was empty, and the neighbors described her walking out of the house in a daze. Diplopia lasting two hours had occurred once.

The patient had noticed her attacks were always worse for several days just preceding the menses, and that as soon as her period started she was free of them for a time. Menses had begun at 15 years and the flow was regular, every 28 days, lasting 3 to 6 days.

One year after the onset of symptoms a glucose tolerance test was performed which revealed exceedingly low values (Table I). This test was performed *the day preceding a menstrual period.* The patient was advised to be hospitalized for study and possible surgery but refused. One morning four months later the patient could not be roused, and thereafter had a clonic convulsion. Her family physician administered glucose solution by vein, and the patient responded. After this incident she consented to hospitalization. *Menses were established four days later.*

Physical examination on admission to the hospital disclosed no remarkable findings. The patient weighed 120 pounds, which was her normal weight. Blood pressure, pulse rate, and temperature were normal.

TABLE I. BLOOD SUGAR VALUES IN MILLIGRAMS PER CENT (MODIFIED FOLIN-WU) FOR ORAL GLUCOSE TOLERANCE TESTS IN CASE OF MRS. E. C.

DATE	FASTING	½ HOUR	1 HOUR	2 HOUR	3 HOUR	4 HOUR	5 HOUR	6 HOUR
Dec. 3, 1953 (28th day of cycle)	29	48	59	66	80			
Apr. 16, 1954 (2nd day of cycle)	67	125	143	150	125	76		
Apr. 20, 1954 6th day of cycle)	43	118	135	223	223	143	86	57

A four-hour glucose tolerance test was done after only a four-hour fast. The values, as shown in Table I, were not abnormal. A six-hour fasting sugar the next day was 55 mg. per cent, and three days later a six-hour glucose tolerance curve showed a fasting value of 43 mg. per cent and a six-hour value of 57 mg. per cent. The patient experienced mild symptoms toward the end of the test. *Both tests were done during the menstrual period.* The following day an upper gastrointestinal x-ray study was performed which showed no abnormalities in the region of the pancreas. During the prolonged fast incidental to this examination (16 hours), the patient lapsed into a semicoma, and a blood sugar value of 45 mg. per cent was obtained. Glucose by vein promptly restored consciousness.

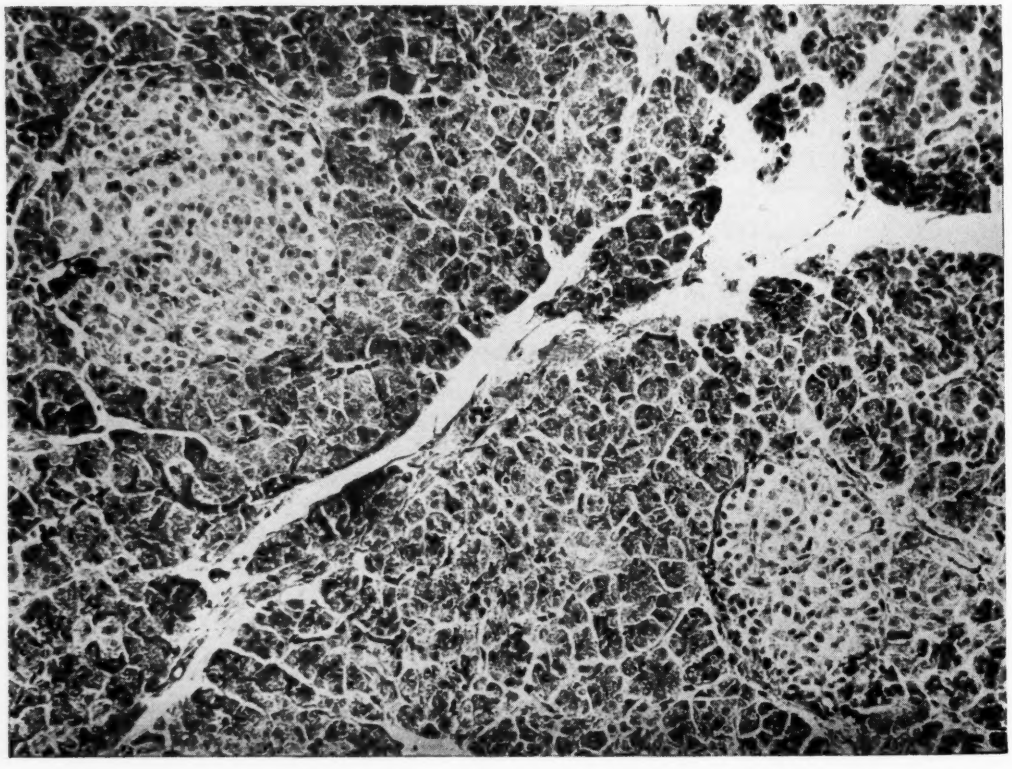

Fig. 1.—Photomicrograph illustrating the type of islet-cell tissue regarded as hyperplastic, encountered in the pancreas in the Case of Mrs. E. C. A normal-sized islet appears in the lower right. (×240; reduced ⅛.)

An electroencephalogram* was reported as showing "no evidence of dysfunction." Blood count, urinalysis, and sedimentation rate were normal, as was a chest x-ray study.

*Performed at the Graduate Hospital of the University of Pennsylvania in Philadelphia, by Dr. Daniel Silverman.

A diagnosis of hyperinsulinism, probably on the basis of an islet-cell adenoma of the pancreas, was made, and an abdominal exploration was carried out on April 26, 1954, by Drs. John Wise and E. Beairsto. Careful exploration of the pancreas in its entirety failed to reveal any evidence of tissue resembling an islet-cell adenoma. The central portion of the head of the pancreas alone could not be adequately palpated. A subtotal pancreatectomy was performed including the entire body and tail from a point immediately above the mesenteric artery. Tortuosity of the splenic artery and vein and their many contributing vessels to the pancreas made a splenectomy necessary.

Immediately following operation, the blood sugar was 280 mg. per cent. The following morning it was 352 mg. per cent, the patient having been given glucose in water by vein during the day. On the second postoperative day the blood sugar was 278 mg. per cent, and thereafter it declined slowly, being 203 mg. on the fourth postoperative day and 176 mg. per cent on the ninth. The patient resumed a regular hospital diet, made a satisfactory and uneventful recovery, and was discharged on the ninth postoperative day. The blood sugar was 143 mg. per cent one month after operation, and 116 mg. per cent in three months. No insulin was ever given.

The resected portion of the pancreas measured 10 by 4 by 0.5 cm. and grossly showed no evidence of tumor formation. Microscopically, the acinar tissue was seen to contain a larger than usual number of islets of Langerhans, there being as many as 6 per low-power field. Many of the islets appeared to be hyperplastic, occupying approximately three-fourths of a high-power field. A diagnosis of *hyperplasia of the islets of Langerhans* was made (Fig. 1).

Comment

The regulation of the blood sugar is a complicated mechanism. Marked hypoglycemia may be due to a variety of causes, its final differentiation sometimes never being determined. In cases of pancreatic islet-cell adenomas, the clinical picture and tolerance tests are helpful but not diagnostic.

The role played by estrogens in lowering the blood-sugar level is not clearly understood, but diabetic women have been shown to have a cyclic fluctuation in their carbohydrate tolerance corresponding to the menstrual cycle, which can be stabilized by administering large doses of the estrogenic hormone.[8] The oral glucose tolerance curves of normal women at various times in the menstrual cycle have been shown by Morton[6] to be lowest in the premenstrual period, and the symptoms of premenstrual tension, some of which are similar to those of hypoglycemia, namely, increased appetite, weakness, fatigue, trembling of the hands, and irritability, can to some extent be relieved by the use of high-protein supplements in the diet.[7]

The elevated estrogen level during the second half of the menstrual cycle has a suppressive action on the anterior pituitary gonadotrophic hormones. Large doses of estrogen are known to suppress the pituitary growth hormone,[4] the same factor which is thought to be the diabetogenic substance and likewise to stimulate production of the hyperglycemic glycogenolytic factor (H.G.F. or glucagon) by the alpha cells of the pancreatic islets.[1, 11]

It can only be surmised that physiologic hypoglycemia during the premenstrual period is due to an estrogen-progesterone imbalance resulting in a relative excess of the estrogenic substance which inhibits the pituitary growth hormone, and thus indirectly disturbs the balance between glucagon and insulin so that blood sugar levels are depressed.

Summary

A case is presented which illustrates marked aggravation of hypoglycemia in the premenstrual period by a functioning hyperplasia of the islets of Langerhans. Oral glucose tolerance curves before and after the onset of menses were totally dissimilar; surgical resection of two-thirds of the pancreas resulted in a reversal of symptoms, and a temporary mild diabetogenic state.

An estrogen-progesterone imbalance is thought to be a factor in premenstrual hypoglycemia; the mechanism whereby a relative excess of estrogens may depress the blood sugar level is briefly discussed.

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SPONTANEOUS SUBARACHNOID HEMORRHAGE IN PREGNANCY

A Case Report

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SPONTANEOUS subarachnoid hemorrhage without hypertension in pregnancy is apparently rare. Thirty-two cases have been reported in the literature since the first by Lazard[1] in 1899. In 1949 deCarle[5] reported 3 cases of subarachnoid hemorrhage complicating normal pregnancy in 15,417 deliveries.

The etiology in the majority of cases is rupture of an aneurysm. This has been demonstrated by angiography or at necropsy.[3-7] Other sources of origin have been arteriovenous angioma, rupture of an arteriosclerotic vessel, septic emboli from endocarditis, and cephalomalacia.

Because of the headaches and convulsive seizures that usually accompany subarachnoid hemorrhage, it must be differentiated from other pathological conditions that produce similar signs and symptoms, namely, eclampsia, epilepsy, uremia, and cerebral lesions. A normal urine analysis and blood pressure are of great aid, but the final diagnosis of subarachnoid hemorrhage is made by the findings in the spinal fluid and the possible demonstration of the lesion with angiogram.

It is because of the difference of opinion in regard to management of these cases, as well as the diagnosis, that the following case is presented.

NCBH No. 165346. P. S. H., a 30-year-old white married woman, had had one previous normal delivery. Her last menstrual period was April 10, 1953, and the expected date of confinement was Jan. 17, 1954. The first prenatal visit was on May 21, 1953, and the history, physical examination, and laboratory findings were within normal limits.

She was seen regularly during the prenatal course and no complications were noted other than excessive weight gain.

On Oct. 28, 1953, at the twenty-eighth week of pregnancy, the patient was admitted to the hospital with a history of one convulsion. She complained of severe frontal and occipital headache with nausea. Physical examination disclosed a blood pressure of 120/70, a 2 plus dependent edema, but was otherwise essentially negative except for findings related to the pregnancy. The laboratory reported a urine analysis, complete blood count, blood sugar and uric acid determinations to be within normal limits. Wassermann and Kahn reactions were negative. X-rays of the skull and chest were considered normal.

The patient was seen in consultation by Dr. Richard Masland, neurologist, and his comments were as follows: "A slight difference in reflexes on the left and right side were

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noted. The reflexes of the left arm and leg were more active than of the right arm and leg. Fine movements were better in the left hand. There was only questionable nuchal rigidity." His final impression was spontaneous subarachnoid hemorrhage.

Dr. Eben Alexander, chief of the Neurosurgical Department, saw the patient in consultation. Lumbar puncture and angiograms were done. The cerebrospinal fluid showed a pressure of 110 mm. of water, tinged with blood, 11,400 crenated red blood cells per cubic centimeter, protein 31 mg. per cent, Pandy's test negative, and the colloidal mastic negative. The angiograms were considered normal. It was his impression that spontaneous subarachnoid hemorrhage had occurred.

During the patient's hospital stay the temperature increased daily to 100.6° F. for the first four days and subsided after that. On the eleventh hospital day the patient was discharged with marked improvement in her condition and without complaints. The prenatal course continued to be uneventful except for weight gain.

The patient was readmitted to the hospital on Dec. 22, 1953, at the thirty-seventh week of pregnancy because of excessive gain in weight of 25 pounds. Physical findings were essentially negative with blood pressure of 110/70, except for 1 plus edema of the ankles. Laboratory findings were within normal limits.

On Dec. 30, 1953, with a favorable cervix and engaged vertex, the membranes were artificially ruptured to induce labor. The first stage of labor lasted four hours and forty minutes. The patient was given saddle block anesthesia (Nupercaine, 2.5 mg.) and was delivered by means of low forceps and episiotomy of a normal female infant who weighed 6 pounds, 3 ounces. The third stage of labor was uncomplicated. The postpartum course was uneventful and the patient was discharged in good condition on the sixth postpartum day.

On return visits at six weeks and six months the patient had been doing well. The blood pressure was normal and her general condition remained good with no evidence of recurrence of the subarachnoid hemorrhage.

Comment

According to Walton's[2] review of the literature in 1953, there have been 32 cases of pregnancy complicated by spontaneous subarachnoid hemorrhage without hypertension. No cases have appeared in the literature since this report. Of the 32 cases, 4 (12.5 per cent) occurred during labor, 18 (56 per cent) occurred before delivery, usually late in the second or third trimester, and 10 (31.5 per cent) occurred during the postpartum period. Six of this last group occurred within the first twenty-four hours after delivery. Thirteen (40 per cent) of the mothers died and 19 (60 per cent) recovered. Walton further states that after the acute phase subsides, the pregnancy should be allowed to proceed to term and that recurrent hemorrhage is no more of a problem during pregnancy than in the nonpregnant state.

Twenty-eight of the 32 cases were reviewed by Conley and Rand[3] in 1951. It was found that the fetal mortality was 26.3 per cent. Fifteen (56.6 per cent) of this group were delivered per vaginam, 7 (25 per cent) were delivered by cesarean section, and 4 (14.3 per cent) died undelivered. The method of delivery was not stated in two cases.

Summary

The case reported is added to the literature in order to show that vaginal delivery with adequate sedation, regional anesthesia, and low forceps delivery is probably a safe method of delivery under these circumstances.

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LUTEIN CYSTS IN NORMAL TWIN PREGNANCY LEADING TO ERRONEOUS DIAGNOSIS OF HYDATID MOLE

A Case Report

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TITUS[1] states that when a patient shows signs suggesting the possibility of hydatidiform mole, such as overenlargement of the uterus with bleeding or brownish discharge, and palpable bilateral ovarian cysts, the diagnosis of mole becomes almost certainly established. The lutein cysts do not always accompany hydatidiform mole but are much more often found in the presence of a chorionepithelioma. He states, however, that there is an exception which also constitutes certain diagnostic points: one must always remember that lutein cysts of pregnancy may form as the result of stimulation from circulating estrogenic hormones. This is more likely to occur in a multiple than in a single pregnancy.

Novak[2] states that, in so far as he has been able to note from laboratory experience, the phenomenon of luteinization of the granulosa or theca cells quite apart from corpus luteum formation occurs in human beings only in association with hydatidiform mole and chorionepithelioma. He mentions that Zondek lays much stress upon the value of positive pregnancy tests obtained from the cerebrospinal fluid of the group with abnormal pregnancies as compared with the negative results in normal pregnancy. Also, according to Novak, typical bilateral multiple lutein cysts have been described as occurring in a case in which there was a normal embryo present in the uterus, the placenta showing only a small microscopic area of hydatidiform disease.

Crossen and Crossen[3] stated that hydatidiform mole, chorionepithelioma, or adenoma of the pituitary can cause marked enlargement of the ovaries, due to the formation of multiple theca-lutein cysts. These cysts are almost always found in association with hydatidiform mole or chorionepithelioma. They state that an Aschheim-Zondek test which is positive in high dilutions is suggestive of the diagnosis, but that it must be remembered that multiple pregnancy will give the same findings, due to the extra amount of placental tissue present. An x-ray is of no value under three months and a negative one even at four months is not conclusive as to the presence or absence of a fetus.

Apparently cases of twin pregnancy complicated by the occurrence of bilateral ovarian lutein cysts, positive spinal fluid Aschheim-Zondek or Friedman tests, negative x-ray findings, and vaginal bleeding in the first trimester are relatively rare, and we have been unable to find any reports of such cases

in the recent literature. The following case is therefore reported to call attention to the necessity of including such a possibility in the differential diagnosis of hydatid mole.

A 25-year-old white housewife, gravida iii, para ii, who was first seen on Sept. 25, 1950, complained of pain present most of the time for the past 12 days in both lower quadrants of the abdomen. The last menstrual period began on June 23, 1950, and she had two episodes of spotting of bright red blood in July, 1950, and a small amount of dark brown vaginal discharge on Sept. 23, 1950. She had also had mild nausea since early in August, 1950.

According to the past history, she had had the usual childhood diseases, and no serious illnesses or operations. Her menstrual history was normal and her two previous pregnancies were uneventful.

On pelvic examination the fundus was anterior, tender, mobile, and measured 11 cm. above the symphysis pubis. The lower segment felt full and the corpus was boggy and a little larger than a 3 months' pregnancy. Both ovaries were tender on palpation and were cystic, and each ovary was approximately 6 cm. in diameter. The general physical examination was normal.

A quantitative Friedman test on Sept. 30, 1950, was reported as positive in the 1 to 10 dilution and doubtful in 1 to 100 dilution. On Oct. 21, 1950, the Friedman test was positive in 1 to 10 and 1 to 100 dilutions but negative in 1 to 700 dilution. A Friedman test done on 4 c.c. of spinal fluid on Oct. 27, 1950, was reported as positive. An x-ray of the pelvis on Sept. 10, 1950, showed no fetus, but a repeat x-ray on Oct. 21, 1950, showed the presence of one fetus estimated by the roentgenologist to be of approximately 17 weeks' gestation.

Because the lower abdominal pain and the enlargement of the ovaries persisted, laparotomy was performed on Oct. 31, 1950. When the abdomen was opened, the uterus was observed to be the size of a 5½ months' pregnancy, and was soft and bluish. Both ovaries were approximately 6 cm. in diameter, and consisted mostly of very numerous small cysts, approximately 1 to 1.5 cm. in diameter, which had yellowish walls and were filled with clear fluid. No uninvolved ovarian tissue was seen. Exploration of the abdomen disclosed no other pathology. A biopsy of the ovaries was taken and frozen sections made, which showed typical multiple lutein and follicular cysts. At this point it was felt that the diagnosis must certainly be either hydatid mole or chorionepithelioma, and, after discussion of the probabilities with the pathologist and with another gynecologist who was present in consultation, and also with the patient's husband who was present in the hospital at the time, it was decided to perform a total hysterectomy rather than to chance leaving a chorionepithelioma in the uterus, or cutting into a chorionepithelioma by doing a hysterectomy. The excised uterus was then opened in the operating room, and was found to contain twin fetuses, each measuring 18 cm. in length. The placentas were fused together and showed no abnormality other than a small area of recent infarction. The uterus itself showed no gross abnormality. Routine appendectomy was then done and the abdomen was closed, leaving both ovaries intact. The patient had a normal postoperative course and was discharged in good condition on the fifth postoperative day.

The pathologist was unable to find any evidence of either hydatid mole or chorionepithelioma on gross or microscopic examination of the uterus or placenta. His final diagnoses were: (1) a uterus measuring 28 by 20 by 15 cm., containing products of conception including twin fetuses; (2) ovarian tissue biopsies showing multiple lutein and follicular cysts.

The patient continued to do well after returning home, and the urinary Friedman test was negative within 2 months of the time of operation. Both ovaries returned to normal size within 3 months after operation.

Comment

It appears that this case might represent either a twin pregnancy which simulated many of the common signs and symptoms often associated with the presence of a hydatidiform mole or chorionepithelioma, or it might possibly represent a hydatidiform mole or chorionepithelioma in conjunction with the twin pregnancy, if the area of hydatidiform degeneration or chorionepithelioma formation was still a small microscopic area in the placenta or in the wall of the uterus and was overlooked by the pathologist in his study of the excised tissues.

The treatment usually recommended in a case where the presence of hydatidiform mole or chorionepithelioma is strongly suspected is immediate evacuation of the uterus and careful examination of the uterine contents. Admittedly the treatment in this case was radical and our decision to perform a hysterectomy rather than a hysterotomy was influenced by two factors: first, the patient already had two normal, healthy children, and both she and her husband expressed a preference for permanent termination of her childbearing ability rather than even a slight risk of leaving a malignant tumor such as a chorionepithelioma in the uterus; second, the consulting gynecologist, who, incidentally, at that time had under treatment a young primipara with metastatic chorionepithelioma, agreed with their opinion. Under these circumstances we felt that the radical, rather than the conservative, treatment was preferable. In retrospect, such a decision is certainly open to question.

Summary

A report is presented of a case of twin pregnancy in which there were many signs and symptoms and clinical laboratory findings commonly associated with the presence of either a hydatidiform mole or a chorionepithelioma, but there was no evidence found in the uterus or its contents of either of these two diseases.

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SUPRAVENTRICULAR TACHYCARDIA IN THE NEWBORN WITH ONSET IN UTERO

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THE ominous foreboding of fetal distress attributed to an irregular and rapid fetal heart rate has been emphasized throughout the years. Indeed, alterations in the fetal heart rate are considered to be the most characteristic sign of intrauterine asphyxia. They are most commonly encountered during labor and it is here that timely and well-calculated intervention may well save the life of an infant.

Discovery of a rapid and irregular fetal rate earlier in the last trimester is a less frequent problem, however. Although it may represent fetal distress and impending intrauterine death, its persistence indicates a different prognosis. Only 12 cases of congenital paroxysmal tachycardia discovered in utero have been reported in the literature. In spite of its infrequency and although paroxysmal tachycardia is relatively benign in the adult, Taussig[5] states that it may be extremely serious in early infancy. If the tachycardia continues for many hours, the infant is liable to suffer from decompensation and may die in cardiac failure. This probably represents one of the explanations of cardiac enlargement and cardiac failure of unknown etiology.[5] The obstetrician must be aware of this condition for it is he who has the first opportunity to make the diagnosis and institute treatment.

Wilburne and Mack[1] have divided the cases of congenital tachycardia into those due to paroxysmal atrial flutter and fibrillation and those of supraventricular origin on the basis of the electrocardiographic findings. The preponderance of cases have been paroxysmal auricular flutter.[2] Three cases of supraventricular tachycardia have been reported, each with its onset in utero.[1, 3, 4]

The following is the fourth such case to be described.

Case Report

A 19-year-old white primigravida was first seen Sept. 11, 1951. Her last normal menstrual period was May 27, 1951, and the estimated date of confinement was March 7, 1952. No significant past history was elicited and findings on physical examination were within normal limits consistent with a fourteen weeks' gestation. Her weight was 112 pounds and the blood pressure was 120/70. The hemoglobin was 82 per cent, red cell count 3.7 million, urine analysis was negative. The Kahn test was negative and the Rh factor was positive. Medications given during gestation were dextroamphetamine sulfate, 5 mg. three times a day, started during the twenty-sixth week because of excessive weight gain (to 135 pounds); ferrous sulfate, 195 mg., and molybdenum oxide, 5 mg., were started during the thirtieth week. At that time the fetal heart tones were first noted to be irregular and the rate over

200 per minute. This finding persisted and on Feb. 19, 1952, an abdominal x-ray failed to demonstrate evidence of fetal anomaly. On March 11, 1952, the fetal heart rate was estimated at 240 per minute.

The patient was admitted to St. Joseph's Hospital, March 12, 1952, in active labor. The fetal heart tones were irregular and too rapid to count accurately. The irregularity was not related to the uterine contractions. Following amniotomy, the heart tones became more rapid but more regular. After seven hours and fifty minutes of labor and under spinal anesthesia, an 8 pound, 4 ounce, male infant was delivered by low forceps from a left occipitoanterior position.

The infant breathed spontaneously, his cry was lusty, his color was slightly dusky, and the heart rate was extremely rapid. Circumoral cyanosis was manifest unless oxygen was administered continuously. An electrocardiogram on March 13 (Fig. 1) demonstrated a nodal tachycardia with a rate of 300 per minute. X-ray failed to reveal any abnormality of the heart or lungs. Vagus stimulation had no effect on the tachycardia. On March 16, digitoxin, 0.05 mg., was given every eight hours for three doses followed by a daily maintenance dose of 0.015 mg. An electrocardiogram on March 17 showed a rate of 215 per minute. On March 20, the rate was 136 and a normal sinus rhythm was present. Oxygen was discontinued March 20 and digitoxin on March 24. The vomiting, which had commenced on March 18, disappeared after discontinuation of digitoxin.

An electrocardiogram on June 7, 1952, demonstrated a slight sinus tachycardia with a rate of 160.

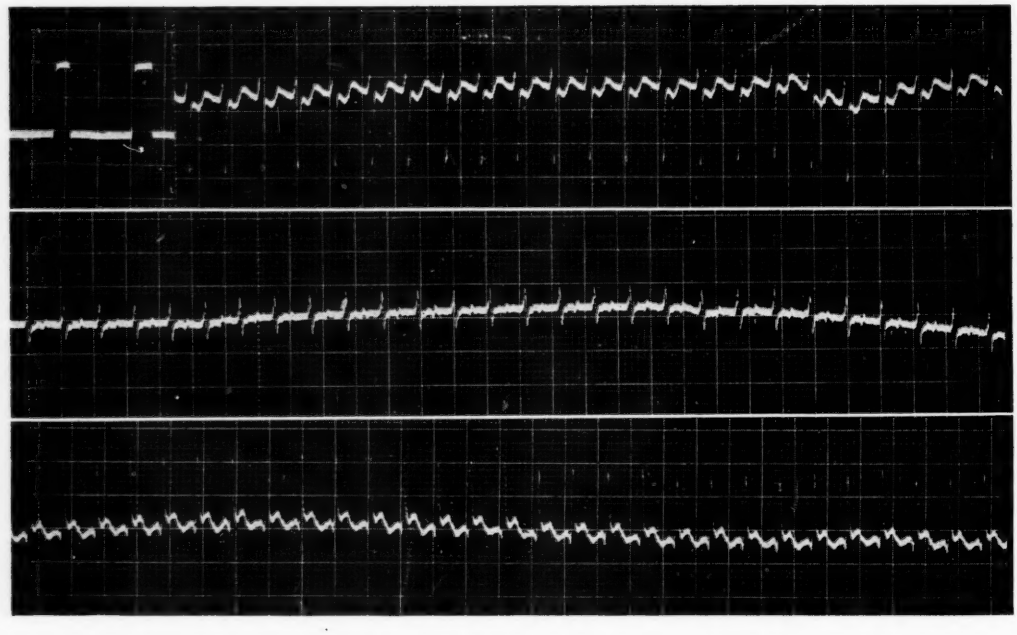

Fig. 1.—Electrocardiogram taken on the first day of life, demonstrating supraventricular tachycardia with a rate of 300 per minute.

Comment

The etiology of congenital tachycardia is obscure. Metabolites in the third trimester, a subclinical electrolyte disturbance, and drugs given the mother during her gestation have been mentioned, but evidence that any of these are causative factors is lacking.[1] In only one of the twelve previously

reported cases was a congenital anomaly of the heart found and there is no evidence that the condition is due to any inherent abnormality in the myocardium.[5]

Anderson and Adams,[2] in their review of the cases of congenital paroxysmal tachycardia, note that the only factor common to all the pregnancies is the high average birth weight of the infants. The birth weights of the infant of this report and that of Wilburne and Mack are consistent with this finding, 8 pounds, 4 ounces, and 7 pounds, 14 ounces, respectively. Probably of greater significance, however, is the fact that this condition has not been reported in premature infants.

The congenital arrhythmias are equally distributed between males and females in contrast to the acquired type which is predominant in male infants.[6] Further, a Wolf-Parkinson-White syndrome has been described in four cases of the acquired arrythmias in infants.[7] This finding has not been reported in the congenital tachycardias.

Paroxysmal tachycardia, as seen in the newborn infant, may be found as early as the sixth month of intrauterine life.[3] Most often, however, it has been detected in the last month of gestation. When found, an abdominal x-ray will help rule out some gross fetal abnormality.

Six of the 13 infants manifested cyanosis and/or dyspnea at birth and 3 of the 4 with supraventricular tachycardia demonstrated these signs.

Electrocardiograms in the latter showed tachycardia with rates of 200,[3] 222,[4] 312,[1] and 300, while in the remainder, flutter and heart block were seen.

Response to therapy varied in the cases of supraventricular tachycardia. The infant treated by Sancetta, Redding, and Haubrich[4] responded to bilateral carotid pressure one hour after delivery and there was no recurrence. That of Garvin and Kline[3] failed to respond to digitalis and after three days quinidine was given. This produced a normal rate and rhythm and was used for three months without recurrence. The case of Wilburne and Mack[1] first responded to digitalis but in each of the recurrences only intramuscular Lanatocide C was effective. Backward and forward failure was present on the sixth day of life. This infant was maintained on digitalis by mouth until 7½ months. In the case here reported, digitalis was effective and there was no recurrence. Of those cases of auricular flutter and heart block which were treated, all responded to digitalis; two infants recovered spontaneously.[2]

The dosage recommended by Nadas and his group[6] is digitoxin, 0.06 mg. per kilogram of body weight, as the initial dose and a maintenance dose of one-tenth this amount for one week or more. Re-examination of the infants at from 3 months to 10 years of age failed to demonstrate any abnormality in all but one child.[5]

Summary

A report of congenital supraventricular tachycardia discovered in utero is presented. This is the fourth such case reported in the literature, bringing to 13 the total number of infants found with congenital paroxysmal tachycardia. The markedly elevated fetal heart rate may be found early in the

third trimester but usually is discovered in the last month of gestation. Cyanosis and dyspnea are often present, cardiac enlargement may be observed, and the electrocardiographic tracings are diagnostic. Cardiac failure has been seen as a sequela. However, digitalis has been effective in all but one of the cases where it has been used, both for the initial attacks and the recurrences. Follow-up studies have demonstrated no abnormal findings in all but one case.

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PREGNANCY AND DELIVERY FOLLOWING OPERATION FOR TETRALOGY OF FALLOT

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WITH the increasing popularization of cardiac surgery in the correction of congenital anomalies, and with the establishment of cardiac surgical centers throughout the country, the end results of the work of these centers may well come into the scope of the obstetrician. In the past, the girl handicapped by severe congenital heart disease either died before she reached adulthood, or, surviving, she was advised against the hazards of marriage and pregnancy. If she did marry despite this advice and subsequently became pregnant, a therapeutic abortion was considered the best solution of the problem in most of the lying-in centers.

Today, however, the picture may be changing. Some of the adolescent girls who were the pioneers for cardiac surgery in 1947 and thereafter have married and are having babies. There are two such reports in the literature to date, of patients who suffered from the tetralogy of Fallot and had a Blalock operation for the correction of this anomaly who have been delivered successfully. Russell[1] had an excellent case report of a pregnancy following the Blalock operation for the tetralogy of Fallot. Less than two months later in the same journal, Olim[2] reported another case. We are herewith presenting what we believe is the third such case recorded.

The tetralogy of Fallot is one of the important congenital malformations of the heart, wherein cyanosis with resultant anoxia is the predominant finding. The lesion consists of pulmonary stenosis, defect of the ventricular septum, overriding of the aorta, and hypertrophy of the right ventricle. Since the pulmonary artery is stenosed, an insufficient volume of blood from the right ventricle reaches the lung bed for aeration. Blalock and Taussig conceived the idea of supplying additional blood by anastomosing a branch of the aorta to the right or left pulmonary artery. This corrective procedure results in considerably less cyanosis and, in many instances, enables the previously severely handicapped cardiac patient to carry on as a normal individual.

The patient whose case is being presented, a 25-year-old primigravida, was seen on June 7, 1953. She gave a history of congenital heart disease, with cyanosis and fainting on the slightest exertion. Because of this, she was taken out of school after the fourth grade and had received all her instruction at home. In 1947, she was referred to the Johns Hopkins Hospital where, after extensive study, a diagnosis of tetralogy of Fallot with right aortic arch was established. On Jan. 23, 1948, she had a Blalock-Taussig operation.

An anastomosis was made between the end of the left subclavian and the side of the left pulmonary artery. Dr. Blalock[3] in his operative report concluded. "The anastomosis was an easy one. After the completion, one could feel an excellent thrill in the pulmonary artery. I thought the anastomosis was a good one." She received 500 c.c. of whole blood, Group A. No Rh typing was done. In addition, she also received 275 c.c. of plasma.

The patient did well postoperatively except for intercostal neuralgia at the operative site. She was instructed gradually to undertake exertions, almost like those of a normal person. In October, 1950, she was admitted to the New York Hospital with a history of fever and fatigue of two months' duration. Numerous blood cultures were taken and all were negative except for one which grew three colonies of *Streptococcus viridans.* She was treated with penicillin every two hours for thirty days. During her last week in the hospital, the spleen became palpable. She was discharged with a diagnosis of possible subacute bacterial endocarditis.

The patient was seen for regular postoperative checkups at the Johns Hopkins Hospital and her progress was considered extremely satisfactory. In October, 1952, she was married. When seen on June 7, 1953, she complained of amenorrhea, fatigue, nausea, and polyuria. The last menstrual period was on April 17, 1953. The menses had started at the age of 11, with an interval of 28 days, and a moderate flow of five days.

Physical examination disclosed an adult white woman with a slight duskiness of the face. There was no clubbing of the fingers. Her weight was 112½ pounds, and the blood pressure 130/64. A well-healed left thoracotomy scar was present with moderate keloid formation. The lungs were clear. The heart was not enlarged. The pulmonary second sound was softer than the aortic sound. A harsh systolic murmur accompanied by a thrill was heard in the third intercostal space. A Grade 3 continuous murmur was heard in the second intercostal space, conducted through to the back on both sides. The liver and spleen were not palpable. Pelvic examination showed a six weeks' pregnancy. In view of her history, the patient was placed under the concurrent care of a cardiologist.

An x-ray examination of the chest and abdomen was performed on July 3, 1953. The only significant finding was marked enlargement of the left hilum, probably due to the engorgement of the pulmonic vessels. A repeat x-ray examination, on Nov. 4, 1953, was essentially the same except for exaggerated pulmonary markings on the left side and some congestion of both bases.

On Sept. 30, 1953, the blood workup of the patient showed that she was Type A, Rh negative, with a negative Kahn test and a hemoglobin of 13.35 Gm. The prenatal course was relatively uneventful until the end of the sixth month of gestation. While shopping, she became dyspneic, cyanotic, and almost fainted. On questioning, she recalled having had a nosebleed or two during that week, with an occasional cough. She had attributed these symptoms to a cold and therefore attached no signficance to them. We, however, felt that these were symptoms of impending heart failure. Examination showed a gain of 4 pounds in 11 days, with a trace of albumin in the urine. The blood pressure was 120/72 and the condition of the heart was relatively unchanged. The patient was placed on a regime of absolute bed rest, on a salt-free diet, and was digitalized. After two weeks in bed, she was permitted bathroom and dining room privileges. From that time until her hospitalization, she was made aware of the fact that her activities were to be confined to the bare necessities. The cough and nosebleeds did not recur.

On Nov. 19, 1953, an Rh antibody determination was done. The titer was reported as 1:1,024. On Dec. 29, 1953, anit-Rh-positive agglutinins were present in the serum in dilutions up to 1:256. Arrangements were made for the hematologist at our institution to be at hand during the delivery, and to be prepared for an exchange transfusion if it were found to be necessary.

X-ray pelvimetry at term confirmed the normal pelvic measurements. The fetus was felt to be small. It was our studied opinon that, in the absence of obstetric indications, this patient should be delivered vaginally, under continuous caudal anesthesia, and that the second stage of labor should be shortened by forceps extraction.

On Jan. 8, 1954, about two weeks before the expected date of confinement, the patient reported that the membranes had ruptured spontaneously. She had no contractions. Rectal examination disclosed an effaced cervix with the occiput at the spines. No membranes could be palpated. The patient was hospitalized and, under continuous caudal anesthesia, an induction was attempted with an intravenous solution of 1:2,500 Pitocin, at the rate of 40 minims per minute. Uterine contractions were instituted every 2 to 3 minutes. During the first hour, the cervix dilated to 2 to 3 cm., but there was no further progress during the next several hours. The blood pressure, pulse rate, and fetal heart tones were carefully observed during these proceedings. No significant variations were observed. After four hours, with no appreciable progress, it was decided to discontinue the intravenous medication.

Sedation was administered and the patient was put to bed. After resting for two hours, she went into labor spontaneously. Her progress was satisfactory. The cervix was completely dilated after a labor of four and one-half hours. The patient was extremely cooperative during labor. Her cardiac status was good. There was no dyspnea or cyanosis and the pulse remained regular and of good quality. She tolerated the caudal anesthesia with no ill effects. A total of 6 c.c. of 2 per cent Xylocaine was given. She also received 100 per cent oxygen, administered by face mask. Intravenous fluids with a vasopressor were readily available. With the aid of a right mediolateral episiotomy, a low forceps extraction was performed and a viable 5 pound 12½ ounce female baby was extracted from the left occipitoanterior position at 10:45 A.M. on Jan. 9, 1954. The infant cried spontaneously. The third stage proceeded uneventfully. The placenta was delivered spontaneously, intact. The episiotomy was repaired in layers. The total duration of labor was five and one-half hours. Penicillin was administered during and after labor and daily during the puerperium.

A Coombs test was done immediately and reported positive. The infant's blood count showed 4 million red blood cells with a hemoglobin of 13 Gm. There were 35 nucleated red blood cells per 100 leukocytes with polychromatic erythrocytes, anisocytosis, and several macrocytes. An exchange transfusion of 500 c.c. of whole blood was administered within three hours after delivery. The baby developed a moderate jaundice which persisted for several days. At discharge, she appeared to be normal, although the blood picture was still depressed.

The patient was observed very carefully after labor for signs of cardiac failure. Blood pressure and pulse readings were taken every fifteen minutes for four hours, and then every thirty minutes for the following twenty-four hours. The blood pressure ranged between 140/64 and 152/70 and the pulse between 78 and 88 per minute. She was allowed out of bed on the first day post partum and was discharged on the seventh postpartum day. Her stay in the hospital was entirely uneventful. She was seen three weeks after delivery. She felt well and offered no complaints. The uterus was well involuted. The cardiac status was unimpaired. A checkup at six weeks showed normal pelvic findings.

Comment

Lund[4] in his report on congenital heart disease as an obstetric problem in 1948 states: "... we must give some thought to the future, particularly as it concerns the surgical treatment of congenital defects ... we are apprehensive about those who are now having surgery for tetralogy of Fallot, and who will wish to have babies ten years from now. Until more information is available, it would seem wise to consider these people as serious cardiac risks, and pregnancy should be undertaken only with extreme caution under constant observation."

Russell,[1] who reported a successful delivery of a patient with the tetralogy of Fallot, following a Blalock operation, stated that a review of the literature, at that time, failed to disclose any previous report of the course of pregnancy in such a patient. He postulated that "with the more widespread use and the increasing success of surgical attacks on congenital cardiac anomalies, it would appear that the problem of management of pregnancy in patients so treated would occasionally confront the obstetrician," and he hoped that the success of cardiac surgery in partially or totally correcting many of the cardiac abnormalities might lead to a revision of current obstetrical practices.

The case which we have just presented is strikingly similar to the one which he reported. Like Russell's, our patient had a relatively uneventful antepartum course except for one episode of incipient heart failure in the sixth month of gestation, for which she was vigorously treated. We were also concerned about the possibility of a recurrence of bacterial endocarditis and employed antibiotics liberally, and we were just as concerned about the immediate postpartum period.

In the main, the essential difference was that, although we were dealing with a primigravida, we also had to contend with an Rh-negative mother who had been sensitized by a blood transfusion and plasma administration. An exceedingly high titer of anti-Rh agglutinins in the last trimester gave us grave concern. Fortunately, however, the baby was born with only a moderately severe erythroblastosis and prompt and efficient treatment by the hematologist gave us a normal baby.

Summary

While no conclusions can be drawn from a series of three case reports, it is nevertheless worthy of note that pregnancy may not be entirely contraindicated in certain types of congenital cardiac anomalies amenable to surgery, despite a moderate calculated maternal and fetal risk.

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URETERAL "KINK" IN PREGNANCY

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IT HAS been amply demonstrated by Traut,[1] Strumpf,[2] and others that dilatation of the renal pelves and ureters and elongation of the ureters are physiologic changes which occur "normally" in pregnancy. These changes usually appear during the fourth month of gestation and regress to normal within four to six weeks following delivery. They are assumed to be due to general relaxation of smooth muscle and to a specific decrease in ureteral peristalsis which occur during pregnancy. These physiologic alterations occur more consistently in the right kidney and ureter presumably because of dextrorotation of the gravid uterus. The dilatation of kidney and ureter during pregnancy has been accepted as a contributing factor in the etiology of pyelonephritis, but little has been documented about this relaxation and elongation of the ureter as being causative in the production of a true ureteral "kink." The following case history is presented for the purpose of demonstrating the clinical course of this unusual condition.

Case Report

Mrs. B. D., No. 8608, a 19-year-old gravida i, para 0, whose estimated date of confinement was Aug. 8, 1954, was first seen as a prenatal patient in our clinic on Feb. 15, 1954. Her initial and subsequent laboratory data were normal, and the progress of her pregnancy was uneventful with the exception of a 25 pound weight gain.

On July 27, the patient was seen on a routine prenatal visit and complained of vague pain in the right flank. Because no positive physical findings were elicited and the urine was entirely negative, the patient was allowed to return home. The following evening, July 28, the patient was resting at home when she developed an increasingly severe and persistent pain in the right flank. She also experienced urinary frequency without dysuria. The pain became so severe that she was admitted to the hospital. There was marked right costovertebral angle and flank tenderness with no muscular spasm. The temperature, pulse, and respirations were normal, and microscopic examination of a concentrated catheterized urine sample showed 2 to 3 white blood cells per high-power field and an occasional red blood cell. No bacteria were seen. A tentative diagnosis was made of right pyelonephritis with possible lithiasis. The patient was treated by bed rest, Demerol for relief of pain, and was observed throughout the night. She continued to experience urinary frequency and increase in right-sided flank pain. The temperature remained normal on the morning following admission, but the pulse had increased to 100 per minute and the patient began to complain of nausea. The uterus was well relaxed, and the fetal heart tones were 140 per minute in the left lower quadrant. The fetus was of term size. Morphine sulfate was administered to control the pain. An x-ray was taken of the kidney-ureter-bladder (KUB) region without demonstrating an opaque renal or ureteral calculus. Immediately thereafter, an intravenous pyelogram showed normal size and function of the left kidney and ureter. There was no visualization of the right kidney pelvis or ureter (Fig. 1). Cystoscopic examination showed a rapid flow of urine from the left ureteral orifice but none from the right. A No. 5 ureteral catheter was introduced into the right ureteral orifice and passed with ease to approximately one-half its length at which time it met an obstruction. At this point there was a sudden rapid flow of concentrated urine through the ureteral catheter. This urine was collected aseptically and cultured for bacteria. Radiopaque solution was injected through the ureteral catheter and a retrograde urogram taken. This demonstrated a marked kink in the midportion of the

Fig. 3.

Fig. 2.

Fig. 1.

right ureter with dilatation of the ureter and renal pelvis proximal to the kink. The right ureter with dilatation of the proximal ureter and kidney pelvis are illustrated in Fig. 2. Although the catheter was not passed beyond the point of obstruction, the patient experienced immediate relief of pain following its introduction. Microscopic examination of the urine collected from the right ureter showed 4 to 6 white blood cells per high-power field. No bacteria were demonstrated by cultural methods.

The patient was returned to the ward and placed in Trendelenburg position with the ureteral catheter in place. Oral fluids were forced and Gantrisin was given for prophylactic purposes. The patient had no recurrence of pain throughout the remainder of the day and night and had an adequate urinary output both from the bladder and from the ureteral catheter. On the following morning her pulse, temperature, and respirations were entirely normal. Rectal examination revealed the cervix to be "ripe" and the vertex dipping into the pelvis. The fetal heart tones were of good quality. Labor was induced by means of a dilute solution of Pitocin administered intravenously. Under constant observation the labor progressed rapidly, and after three and one-half hours saddle block anesthesia was administered and the patient was delivered of a 3,047 gram male child who was entirely normal. The patient was returned to the postpartum ward and again placed in Trendelenburg position. There was no recurrence of right-sided pain. Routine postpartum care and perineal hygiene were given in addition to gentle catheter irrigations twice daily. The postpartum course continued uneventfully, and on the second postpartum day a second retrograde pyelogram disclosed a persistence of the hydronephrosis and hydroureter on the right side.

The patient remained afebrile and repeated urine cultures from the right ureter were negative. On the third postpartum day the catheter was removed and the patient continued on bed rest in Trendelenburg position. She continued to be free of symptoms and was allowed to ambulate on the following day. Urine obtained by catheterization on the fourth day contained many white blood cells although Gantrisin had been continued up to that time. Because of this, Gantrisin was discontinued and Chloromycetin was administered orally. On the eighth day post partum, the urine contained only 5 to 6 white blood cells per high-power field. The patient was discharged from the hospital and advised to continue the Chloromycetin medication for four additional days. She was instructed to return in one week for urinalysis and intravenous pyelography.

A urine sample obtained by catheterization on the thirteenth postpartum day contained only 1 to 3 white blood cells per high-power field. Intravenous pyelography at this time revealed both kidney pelves, the calyces, and the ureters to be well outlined with no evidence of the previous right ureteral kink. Illustration of the right kidney and ureter without kink is seen in Fig. 3. The patient had been entirely asymptomatic since her discharge from the hospital and at the last examination, eight weeks post partum, was having no further difficulty.

Summary

The case history is presented of a patient who had a ureteral kink during the thirty-ninth week of pregnancy which resulted in marked hydronephrosis. Kinking may occur in pregnancy because of physiologic relaxation and elongation of the ureters. Ureteral kink should be considered in the differential diagnosis of acute progressive flank pain in pregnancy. Prompt diagnosis, drainage of the affected ureter, and induction of labor (if at term) as soon as is feasible will allow resolution of the kink early in the postpartum period.

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REPEATED SPONTANEOUS VERSION OF A DEAD FETUS

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(From the Obstetrical Service of the Burtonwood Air Force Base Hospital, Warrington, England)

THE occurrence of spontaneous cephalic version of the fetus in utero is a well-known and frequent phenomenon. Eastman[1] presented statistics collected by Schroeder, based upon several hundred thousand cases, which indicate that the head presents in about 95 per cent and the breech in 3 to 4 per cent of all pregnancies at or near term. Earlier in pregnancy, however, breech presentations occur more frequently. Ryder[2] has stated that at the thirtieth week one pregnant woman in every six has a breech presentation, while Vartan[3] has presented the incidence as one in four and regards it as a normal occurrence at certain stages of pregnancy. The great majority of these breech cases at the thirtieth week later undergo spontaneous cephalic version, usually about the thirty-second week but often later. Those who are opposed to external cephalic version have used this fact as a cogent argument in support of their stand.

Despite the general acceptance of the fact that the fetus does turn within the confines of the uterine cavity, little is actually known as to the cause of the version. Most obstetrical textbooks which discuss the subject do not offer an explanation for its occurrence. In general, however, it is agreed that the movements of the fetus per se are essential to spontaneous version, and according to Stabler[4] the kicking of the fetus is the most powerful factor in determining the predominance of head presentations.

In 1951, however, Abt[5] of the Basel University Clinic reported two cases of spontaneous change of position of a dead fetus occurring at the thirty-second and thirty-fourth week of gestation, respectively. In both cases the rotation was from head to breech and followed unsuccessful attempts at induction of labor. He refers to Naujoks' sign—the stability of fetal position in x-rays taken at intervals—which has long been considered on the European continent as diagnostic of intrauterine death. He points out that his two cases show that it is not a reliable sign.

Recently, we have had occasion to deliver a patient whose fetus died in utero and whose history refutes once again the argument that a live fetus is a necessary prerequisite to spontaneous version late in pregnancy.

Case Report

The patient was a 32-year-old white woman, gravida v, para iii, who was first seen at the Burtonwood Air Force Base prenatal clinic on Feb. 23, 1954. Her obstetrical history showed a spontaneous abortion at six months in 1939 followed by three normal deliveries of living babies. The last two deliveries were both by the vertex, although the babies had been presenting by the breech one week prior to birth. In 1944 she had an appendectomy, right oophorectomy, and uterine suspension.

Fig. 1. Fig. 2.

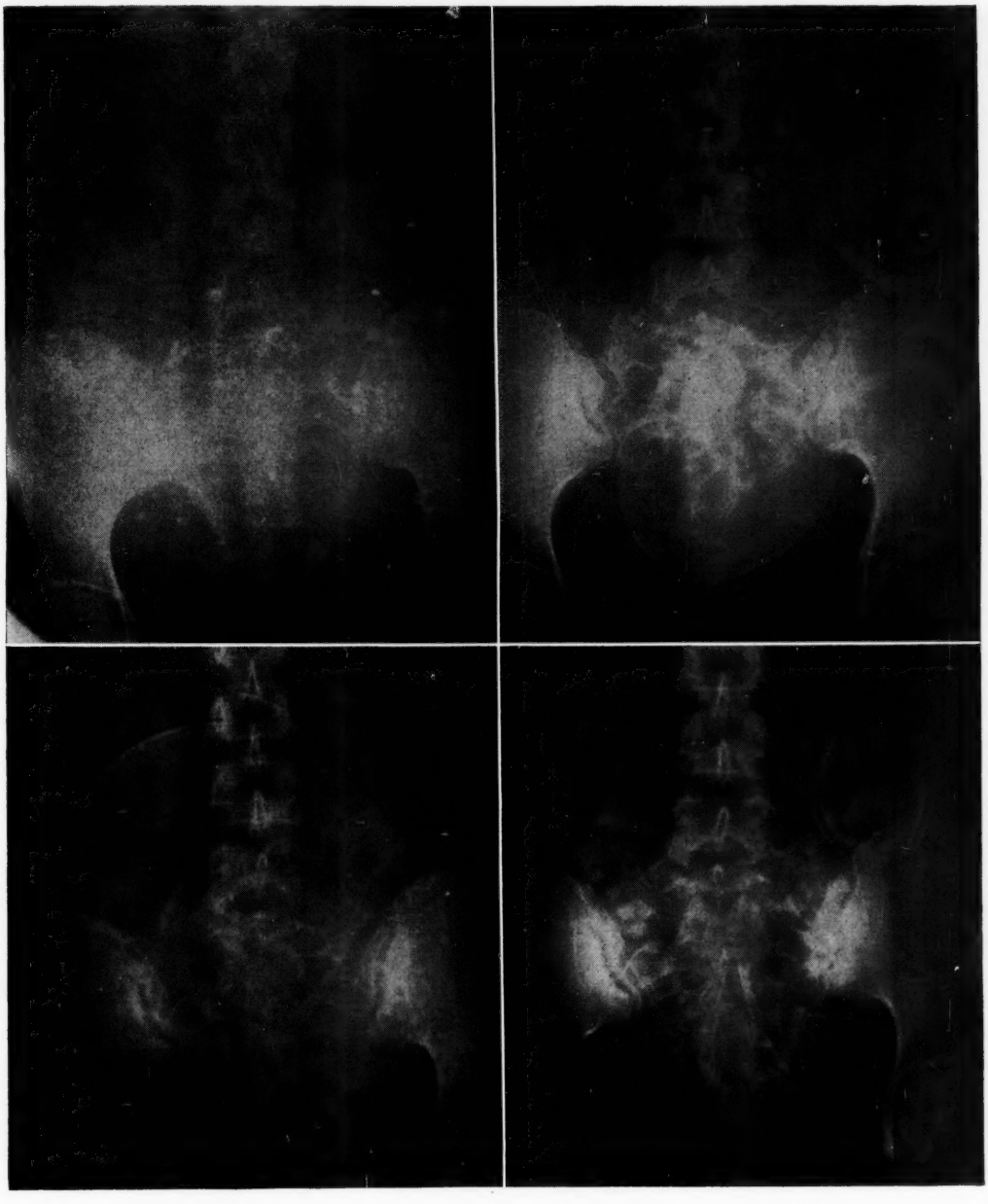

Fig. 3. Fig. 4.

Fig. 1.—X-ray taken on June 6, 1954, about 36 hours after cessation of fetal movement, shows fetus in frank breech position with spine to the maternal right. No signs present to suggest fetal death.

Fig. 2.—Re-examination 3 days later shows fetus to have turned so that the vertex is now presenting. There is slight abnormal flexion of the cervical spine and minimal overriding of the skull bones.

Fig. 3.—A repeat film on June 14, 1954, shows unmistakable signs of fetal death with overriding of the bones of the skull and abnormal flexion of the spine. The fetus is now in the frank breech position again, this time with the spine on the mother's left.

Fig. 4.—X-ray taken on June 28, 1954, in early labor. The fetus is markedly deformed. The lie is transverse. There is an acute kyphosis in the lower thoracic spine and this portion is presenting.

The patient's last menstrual period was on Oct. 5, 1953, and her expected date of confinement was July 12, 1954. She was first aware of quickening one week prior to her initial visit. Physical examination showed a normal pregnancy of approximately 20 weeks' duration. Systemic examination was essentially negative. The pregnancy continued uneventfully except for an occasional attack of dizziness. On June 6, 1954 (the thirty-fifth week of pregnancy), the patient reported that she had felt no fetal movements for thirty-six hours. The fetal heartbeat was not heard. An x-ray the same day showed a single fetus in the frank breech position with the spine to the maternal right (Fig. 1). The appearance was compatible with the clinical age of thirty-five weeks. There was no abnormal flexion of the spine or overriding of the skull bones to suggest fetal death. A repeat x-ray three days later showed the fetus to have turned so that now the head was presenting (Fig. 2). At this time there was noted an abnormal flexion of the cervical spine and minimal depression of the bones of the fetal skull. A further x-ray taken eight days after the original one showed unmistakable signs of fetal death with a definite Spalding's sign and acute flexion of the spine (Fig. 3). The fetus had reverted to the frank breech position again, this time with the spine on the mother's left.

The patient entered the hospital two weeks later at 4 A.M. on June 28, 1954, pains having commenced at 2:30 A.M. There had been a brownish discharge present for the previous two weeks. On admission the membranes were intact, the uterine contractions were irregular, and the presentation of the fetus could not be made out with certainty (Fig. 4). At 7 A.M. the pains were occurring every five minutes, the presenting part was in the midcavity and the cervix was 2 fingers dilated. At 10:30 A.M. the membranes were artificially ruptured under nitrous oxide-oxygen-ether anesthesia. At 1:35 P.M. a macerated male fetus was born spontaneously as a shoulder presentation, after a left mediolateral episiotomy had been performed. The third stage was normal as was the puerperium, and the patient was discharged from the hospital on July 2, 1954. The cause of the intrauterine death was not ascertained.

Comment

Many theories have been advanced to explain why the fetus presents most often by the head but none have been generally accepted. Taussig[6] states that with a normal pelvis, normal uterus, and a single fetus, gravity and the kicking movements almost always tend to produce a head presentation. The fact that spontaneous cephalic version will take place in a woman confined to her bed for some coincident condition seems to disprove the gravity theory. According to Eastman,[1] perhaps the most tenable theory is that of accommodation, which bases the predominance of head presentations on the pyriform shape of the uterus. The fundus corresponds to the larger pole while the lower uterine segment represents the smaller pole. The fetal head at term is larger than the breech but less bulky and less mobile than the entire podalic pole of the fetus—that is, the breech together with its flexed extremities. Before the thirty-second week of pregnancy the total mass of the fetus is small in relation to the total amniotic fluid mass and the uterine walls are not closely applied to the fetus. At about this time, however, the fetal mass increases disproportionately in relation to the amniotic fluid mass and the uterine walls are brought in close apposition to the fetal parts. It is at this time that the effect of the pyriform shape of the uterus is thought to be exerted. If the fetus has been presenting by the breech it changes its polarity in order to make use of the roomier fundus for its bulkier and more motile podalic pole. In the words of Polak,[7] "It would have been a head, if it could have been a head." The presence of placenta previa, cornual-fundal implantation of the placenta (Stevenson[8]), congenital ab-

normalities of uterine shape, multiple gestation, hydrocephalus, extension of the fetal legs, and other conditions which alter either the polarity of the uterus or the shape of the fetal mass might prevent the version.

It has been assumed therefore that when spontaneous version occurs in utero it is a process of the fetus accommodating itself to its intrauterine dwelling. Under these circumstances the fetus has been considered to play an active part in the version by means of a series of varied movements, the most significant of which is the paddling or kicking action of the extremities. It has been shown that in those breech presentations which resist either spontaneous or manual attempts at version the attitude of the fetal legs is consistently extended. It is this attitude which permits the least amount of activity of the extremities. Both Vartan[3] and Stein[9] in analyzing skiagrams have pointed out that, when the fetus eventually turns, the attitude is most often flexion or semiflexion, whereas when the fetus resists version the attitude is most often extension. The uterus and the liquor amnii have been thought to play a passive part, or at the most a minor role. Usually when the fetus dies in utero there is a resorption of amniotic fluid and it may be the subsequent reduction in liquor which causes the fetus to be held in a fixed position. In the case presented there was no evidence either clinically or roentgenologically of much decrease in the amount of liquor.

Further in the case presented the spontaneous cephalic version was followed by reversion. While reversion of the fetus occurs often (in 33.3 per cent of cases, according to Ryder[2]) following external cephalic version, it is believed to be an unusual occurrence after spontaneous version. From this it can be inferred that if the conditions necessary for spontaneous cephalic version are not present, then reversion may take place after an external version prematurely performed. This fact suggests that the obstetrician is not always as clever as the fetus in deciding when the change of position should be performed.

Summary

A case of spontaneous version of a dead fetus at the thirty-fifth week of pregnancy has been presented. The initial movement was from extended breech to head but this was followed in a few days by reversion back to an extended breech presentation. The macerated fetus was delivered three and one-half weeks after the intrauterine death, as a scapular presentation. It appears, therefore, that the presence of a living active fetus is not necessary for the phenomenon of spontaneous version.

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Department of Reviews and Abstracts

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Selected Abstracts*

The Medical Journal of Australia

Vol. II, No. 13, September 25, 1954.

*Davis, J., and Meares, S. Devenish: Preliminary Report on an Investigation of Fetal Electrocardiography and Fetal Stethography, p. 501.

Davis and Meares: Investigation of Fetal Electrocardiography and Fetal Stethography, p. 501.

The introductory paragraph mentions that the information gained by fetal electrocardiography and fetal stethography may be obtained by x-ray or clinical means. The article proceeds to describe how one may diagnose pregnancy as early as the seventeenth week, or determine breech or vertex presentation, or whether a multiple pregnancy exists. Stethography may supplement the fetal electrocardiograph in the last trimester. The authors have been able to obtain recordings in nine-tenths of the subjects tested. The use of their apparatus, a six-channel electroencephalograph, is described.

The reviewer agrees with the author that the information secured may be derived in other ways and may add that some of the other methods are more readily available, less difficult to use, and probably more reliable than those of the authors. Fetal electrocardiography and stethography are interesting but of no significant value to the obstetrician.

ARTHUR PERELL, M.D.

Vol. II, No. 14, October 2, 1954.

*Bellingham, F. A.: Induction of Labour, p. 545.

Bellingham: Induction of Labour, p. 545.

The author discusses the results of combined medical and surgical induction of labor at the Woman's Hospital, Crown Street, Sydney, from July to June, 1950-1951 and 1952-1953. There were a total of 9,255 viable infants born in that period with induction in 3.4 per cent of the cases. Medical induction consisted of enema and castor oil in all cases and occasionally stilbestrol, estrogens, quinine, or Pitocin. Surgical induction, used prior to or after medical induction, is performed by artificial rupture of the membranes. Low ruptures are produced with a Howard Kelly clamp or a similar instrument while the high amniotomies are done with a Drew-Smythe catheter.

The efficacy of both types of rupture in primigravidas and multigravidas is compared with apparently better results, regardless of parity, with the low rupture technique. Indications for induction are tabulated, pre-eclamptic toxemia being the most common.

*Titles preceded by an asterisk are abstracted below.

The fetal mortality was 3.4 per cent. The section rate was 1.9 per cent. The average time from rupture of the membranes to the end of the third stage was 33.1 hours. Multiparity did not improve the efficiency of the method. There were no maternal deaths.

This routine for the induction of labor is advocated in some of the clinics in this country. Those practitioners who are not perturbed by adding the complication of prolonged rupture of the membranes and potential infection to patients who require induction may agree with the author that medical and surgical induction as described in this monograph is a safe procedure.

ARTHUR PERELL, M.D.

Vol. II, No. 16, October 16, 1954.

Ellery, R. S.: Frigidity and Dyspareunia, p. 626.

Vol. II, No. 18, October 30, 1954.

*Clemens, Kathleen, and Walsh, R. J.: The Frequency of Immunization of Rh-Negative Women by Rh Antigens, p. 707.

Clemens and Walsh: Frequency of Immunization of Rh-Negative Women by Rh Antigens, p. 707.

This report concerns Rh-negative mothers sensitized against Rh antigens and variations of this sensitivity produced by subsequent gestations. The material was collected from random reports of 5,694 Rh-negative maternal blood samples submitted to the Red Cross Blood Transfusion Service by some of the hospitals in New South Wales. These were examined by the methods proposed by Race and Sanger.

Analysis of the data indicated that the following percentages would show immunization with pregnancy (parenthetical figure is percentage of Rh-negative women with Rh-positive husbands who demonstrate Rh antibodies): 0.6 per cent (0.7 per cent) during the first pregnancy, 6.6 per cent (7.9 per cent) during the second pregnancy, 11.6 per cent (14.0 per cent) during the third, 17.6 per cent (21.2 per cent) during the fourth, 25.4 per cent (30.6 per cent) during the fifth pregnancy, 27.5 per cent (33.2 per cent) during sixth or subsequent pregnancies. These figures are proposed without consideration of the genotype of the husband. This, of course, will have an important influence on the percentage of immunizations produced, and the author discusses this and other pertinent factors in the publication.

ARTHUR PERELL, M.D.

Vol. II, No. 20, November 13, 1954.

Hughes, E. Kent: Induction of Labour, p. 787.

Die Medizinische

No. 10, March 6, 1954.

Kapp, R. K.: On Radiotherapy in Gynecological Carcinoma, p. 309.

*Schubert, R., and Peters, H.: Jaundice and Pregnancy With Special Consideration of Infectious Hepatitis, p. 315.

Schubert and Peters: Jaundice and Pregnancy With Special Consideration of Infectious Hepatitis, p. 315.

Among 321 cases of infectious hepatitis and homologous serum jaundice in women, the authors saw 26 cases in pregnancy. Eighteen of these occurred in the last trimester. Despite the preponderance of incidence in the last trimester, this disease is not due directly to pregnancy but rather to an increased hepatic load which predisposes to infection in epidemic areas. Infectious hepatitis in pregnancy appears to be less rare than was previously thought.

Under the usual therapy for the disease disregarding pregnancy, the prognosis for both mother and fetus is generally good. Complications noted in this series were acute yellow atrophy in two cases, one of which ended in death for both mother and fetus; the other produced a macerated, immature, stillborn infant. Recovery followed evacuation of the uterus. There were three cases of prematurity with good fetal and maternal results. One baby died of pulmonary complications shortly after birth. This was apparently not attributable to the mother's disease. In no case in this series was there any transmission of the disease from the mother to the infant.

Treatment consists generally of diet to protect the liver, cortisone, and hormone therapy if indicated by threatened abortion. Interruption of pregnancy is considered only in cases of hepatic coma.

WALTER F. TAUBER, M.D.

No. 13, March 27, 1954.

Doering, K.: On the Question of a Decrease of Intellectual Ability During Menstruation, p. 425.

No. 16, April 17, 1954.

Domanig, E.: Measures to Reduce Surgical Risks, p. 540.

No. 18, May 1, 1954.

Cramer, H.: An Evaluation of New Methods for the Early Diagnosis of Gynecological Carcinoma, p. 642.

Finkbeiner, H.: The Importance and Extent of Prenatal Care, p. 652.

No. 20, May 15, 1954.

*Schwenzer, A. W.: Maternal Paralysis Due to Traumatic Childbirth, p. 709.

Schwenzer: Maternal Paralysis Due to Traumatic Childbirth, p. 709.

Traumatic paralysis of the lower extremities due to injury in childbirth is rare. Reports vary from 9 cases in 19,000 to 7 in 45,000.

The peripheral nerve most often involved is the peroneal, although others may also be affected. The etiological factor is usually trauma to the lumbosacral trunk where it crosses the linea terminalis. This often occurs in prolonged and difficult labors with borderline cephalopelvic disproportion. Pressure of the baby's head causes damage to the nerve trunk. Thus in left occipitoanterior and right occipitoposterior presentations, symptoms will be on the right side, and in right occipitoanterior and left occipitoposterior presentations, on the left. Occasionally, difficult forceps deliveries may be responsible. In such cases, the opposite nerve trunk is involved. Since symptoms do not usually appear until after delivery and since this condition occurs also in spontaneous delivery, no prophylactic measures can be advised.

WALTER F. TAUBER, M.D.

No. 21, May 22, 1954.

Tietze, K.: Hormonal Versus Other Therapy for Menopausal Complaints, p. 751.

No. 24, June 12, 1954.

Lehmacher, K.: The Dangers of Radium Therapy in Uterine Carcinoma, p. 844.

Stienen, G.: On the Incidence of Erythroblastosis and Hemolytic Disease of the Newborn in ABO Incompatibility, p. 849.

No. 25, June 19, 1954.

*Frangenheim, H., and Schenk, G.: The Treatment of Tuberculosis of the Female Genital Tract With PAS, Streptomycin, Thiosemicarbazone, Isonicotinic Acid Hydrazide, p. 875.

Kloeppner, K.: Study on Labor Pain, p. 885.

Frangenheim and Schenk: Treatment of Tuberculosis of the Female Genital Tract With PAS, Streptomycin, Thiosemicarbazone, Isonicotinic Acid Hydrazide, p. 875.

The use of PAS, streptomycin, thiosemicarbazone, and isonicotinic acid hydrazide in genital tuberculosis is discussed. The authors deal with a series of only 22 cases. They find fairly good results in that progressing cases are usually arrested, some even reversed. The main advantage of chemotherapy, however, lies in making cases of adnexal tuberculosis more amenable to surgery, making surgery less hazardous in terms of tubercular sequelae, and reducing the amount of surgery required for cure.

WALTER F. TAUBER, M.D.

No. 26, June 26, 1954.

Doutenwill, W., and Finke, L.: Toxoplasmosis in Pregnancy and Specificity of Serological Examination of the Infected Mother, p. 906.

No. 27/28, July 10, 1954.

Luettge, W.: Changed Indication and Technique in Cesarean Sections, p. 945.
Cordua, R.: Routes of Metastases of Carcinoma of the Cervix, p. 947.

No. 29/30, July 24, 1954.

*Soost, H., and Wiemer, J.: Methylandrostenediol, an Androgen for Gynecology, p. 1010.

Soost and Wiemer: Methylandrostenediol, an Androgen for Gynecology, p. 1010.

The use of this preparation which, chemically, differs little from androsterone is discussed. It appears to have the beneficial effect of androgen in mammary carcinoma in that it reduces pain and slows down metastases. The dosage suggested is 200 to 300 mg. per week. The authors have also used lower dosages (50 mg. every other day for three days or four doses at intervals of several months) for menopausal symptoms. Similar dosage every month has been used for dysmenorrhea and the drug also appears to be of value in suppressing lactation.

Despite the fact that it has so many androgenlike properties, this medicament—when given in therapeutic dosages—does not seem to cause the appearance of male characteristics or the suppression of female ones. The only contraindication mentioned is pregnancy.

WALTER F. TAUBER, M.D.

No. 31/32, August 7, 1954.

Wunderlich, E., and Stoll, P.: The Diagnosis of Extrauterine Gestation in Practice, p. 1031.

No. 35, August 28, 1954.

*Roemer, H., and Vollmer, E.: Pituitary Gland Implantation in the Treatment of Disturbances of the Cycle. (Part I), p. 1142.
Rupp, H.: Origin, Prevention, and Treatment of Puerperal Mastitis, p. 1147.

No. 36, September 4, 1954.

*Roemer, H., and Vollmer, E.: Pituitary Gland Implantation in the Treatment of Disturbances of the Cycle. (Part II), p. 1199.

Roemer and Vollmer: Pituitary Gland Implantation in the Treatment of Disturbances of the Cycle. (Parts I and II), pp. 1142 and 1199.

The authors discuss the use of anterior pituitary implants in the treatment of menstrual dysfunction. The cases discussed fall into the following categories: postpartum, following head trauma, pubertal, and psychogenic. In all classes, they obtained the best

results if there was no organic pituitary disease. In other words, they are not dealing with such conditions as Sheehan's disease. Most of their patients have trunk adiposity and some other glandular disturbances.

In the first group, they discuss 100 cases with 63 permanent cures. The authors feel that some irreversible structural changes took place in the remaining 37. They deal with 24 psychogenic cases of which 16 were successfully treated. Most of these occurred around puberty. Fourteen showed adiposity, while the remaining 10 had anorexia nervosa. The 8 patients who did not respond to the implantation had either gone so long without treatment that involution of the genital tract had occurred, or the psychological trauma was still present.

The authors feel that all their cases represent functional disturbances of the hypophysis and diencephalon. The gonadotropin excretion was shown to be normal in their successful cases. The technique that they recommend is the implantation of at least five whole pig pituitaries under the fascia lata. These implants maintain function for from four to six months and it is felt that this permits endogenous gonadotropin activity to be reestablished.

WALTER F. TAUBER, M.D.

No. 37, September 11, 1954.

*Weyers, K.: On the Treatment of Sterility and Infertility in Uterus Didelphys, p. 1246.

Weyers: Treatment of Sterility and Infertility in Uterus Didelphys, p. 1246.

Nonfusion and malfusion of the Müllerian duct gives a poor obstetrical prognosis, the chief factors being sterility and high abortion and prematurity rates. If such patients do go to term, there is a high incidence of premature rupture of the membranes, abruptio placentae, retained placenta, uterine inertia, and malpresentation.

After reviewing the literature, the author presents three cases. One was untreated and went to term successfully. The other two had normal children following plastic operations of the uterus.

WALTER F. TAUBER, M.D.

No. 41, October 9, 1954.

*Schmiemann, R.: Can Menopausal Symptoms be Treated Etiologically? p. 1372.

Kolowrat, F.: The Use of Guiacol-glycerin Ether as a Muscle Relaxant in Operative Gynecology, p. 1382.

Schmiemann: Can Menopausal Symptoms be Treated Etiologically? p. 1372.

The author feels that a considerable part of the symptoms associated with the menopause are due to the activity of the pituitary, freed from control by the ovarian hormones. With this rationale he exposes the hypophysis and diencephalon to ultrashort wave radiation. He feels that he has obtained good results with this treatment. Four illustrative cases are presented.

WALTER F. TAUBER, M.D.

No. 44, October 30, 1954.

Siedentopf, H.: Analgesia for Cesarean Section, p. 1475.

Münchener Medizinische Wochenschrift

Vol. 96, No. 39, September 24, 1954.

Hollenweger-Mayr, B., and Thye, A.: Oestrogynaedron[R] for Women Wearing Pessaries, p. 1127.

Vol. 96, No. 40, October 1, 1954.

*Heim, K.: Abruptio Placentae, p. 1151.

Scheuer, F.: Menopausal Arthropathies, p. 1156.

Engel, G.: The Role of Prolonged Wearing of a Pessary as a Contributing Factor in Carcinogenesis, p. 1159.

Michels, B., and Schanz, G.: The Oral Use of Buffered Penicillin in Gynecology and Obstetrics, p. 1164.

Drescher, H.: Clinical Experience With the Spasmolytic Agent, Avacan[R] in Obstetrics, p. 1164.

Heim: Abruptio Placentae, p. 1151.

The etiology, clinical course, pathology, and pathological physiology of premature separation of the placenta are reviewed.

In treating this complication of late pregnancy, the author advises conservative management. He divides cases into mild, moderate, and severe. Selected mild cases are considered amenable to induction of labor with rupture of the membranes and oxytocics. He quotes Weymeersch and Snoeck (1937) showing that the lowest maternal mortality was obtained in moderate and severe cases with spontaneous vaginal delivery (2.4 per cent). This, however, is compared to such hazardous operative interventions as version and extraction. A summary of the world literature up to 1936 shows a 27 per cent over-all maternal mortality with abdominal operations (cesarean section 16.4 per cent, hysterectomy with pregnancy intact 21 per cent, Porro section 35.3 per cent, vaginal cesarean section 45.4 per cent, postpartum hysterectomy 88.8 per cent). This is compared to figures varying from 2.2 to 5 per cent for conservative management. No mention is made of operative statistics since the advent of improved blood banks, antibiotics, improved anesthesia, and fibrinogen.

WALTER F. TAUBER, M.D.

Vol. 96, No. 43, October 22, 1954.

Mikulicz-Radecki, F.: Anuria in Obstetrics and Gynecology, p. 1247.

Vol. 96, No. 47, November 19, 1954.

Naujoks, H.: Diagnosis and Treatment of Placenta Previa, p. 1377.

The New England Journal of Medicine

Vol. 251, No. 6, August 5, 1954.

*Hershenson, Bert B., Isaac, Simon J., Romney, Seymour L., and Reid, Duncan E.: New Sedative (Antipsychomotor) Drug Useful in Labor, p. 216.

Hershenson, Isaac, Romney, and Reid: New Sedative (Antipsychomotor) Drug Useful in Labor, p. 216.

This is a preliminary report on the use of Thorazine (chlorpromazine) in labor based on the study of 100 cases. The group studied was divided equally between primiparous and multiparous patients with uncomplicated pregnancies. The drug was given following oral or rectal administration of Seconal early in established labor for the production of amnesia and analgesia from the time at which the patient first complained of pain. The medication was repeated at two-hour intervals, or more often if the patient showed any increase in psychomotor activity. Total dosage was limited to approximately 100 mg. per patient. The number of doses varied from a minimum of one to a maximum of 13. The average and usual individual dose was 12.5 mg. Anesthesia used for delivery was of the inhalation type in most instances.

The authors report that the emergence phase was pleasant and uneventful. The condition of the babies at birth was satisfactory, and they exhibited spontaneous respiration at or soon after delivery in 96 per cent of the cases. The value of the drug appears

to be that it is a pharmacologic antagonist to such psychomotor hyperactivity as is periodically encountered with the combined use of barbiturates and is useful for intrapartum analgesia and amnesia.

DOUGLAS M. HAYNES, M.D.

Vol. 251, No. 8, August 19, 1954.

*Buxton, C. L., and Van de Wiele, Raymond: Wedge Resection for Polycystic Ovaries, p. 293.

Buxton and Van de Wiele: Wedge Resection for Polycystic Ovaries, p. 293.

From the files of the Sloane Hospital for Women, the authors collected 40 cases of polycystic ovaries in which operation had been performed. The study was undertaken with the objective of answering two basic questions: whether polycystic ovaries occur with menstrual disturbances other than amenorrhea; and whether such ovaries constitute a coincidental finding in cases of extragenital endocrine disease such as the adrenogenital syndrome. All patients who at laparotomy were found to have polycystic ovaries were included in this study regardless of preoperative symptoms. Amenorrhea or oligomenorrhea was present in 30 of the patients; 3 had regular cycles, and 7 gave a history of menometrorrhagia. Twenty-seven of the 40 patients studied demonstrated some degree of hirsutism. Thirteen patients had at least one endometrial biopsy. In patients with amenorrhea, atrophic, inactive proliferative, or no endometrium was obtained. No case was noted in which the endometrium showed a secretory pattern. The endometrial response to estrogen was normal in all patients. Total 17-ketosteroids were tested in 27 cases, and in 23 the values fell within normal limits. No differences were noted in total 17-ketosteroid excretion between patients with hirsutism and those without this feature. Column chromatography with subsequent identifications of the isolated steroids by infrared analysis was used to bring about fractionation of the 17-ketosteroid complex in 7 of these patients; normal values were found in all but one. Wedge resection was done on 27 hirsute patients, and follow-up reports were obtained on 25 of these. In only one did the abnormal hair distribution revert to a normal pattern; 4 patients noted an increase in the rate of hair growth after operation. In the remainder, there was no change of the hair distribution following wedge resection. The menstrual cycle was evaluated in 28 patients; of these, 20 were cured, 4 were improved, and 4 unaffected. The authors believe that the so-called Stein-Leventhal syndrome is probably due to some complex and poorly understood dysfunction of the pituitary-adrenal-ovarian axis. Therapy aimed at producing disappearance of the hirsutism appears doomed to failure in most instances. The menstrual disturbances and evidences of anovulatory cyclical phenomena seem to be cured by wedge resection in a high percentage of cases in which the ovary seems to be the main offender, but the procedure is ineffective when the main site of physiologic function is the adrenal gland. From their data the authors conclude that any type of menstrual disturbance may occur with polycystic ovaries, although usually the menstrual picture is that of amenorrhea. Whenever there is elevation of the 17-ketosteroid excretion level or when adrenal depression is produced by cortisone and the patient previously amenorrheic resumes menstruation and ovulation during cortisone therapy, the authors believe that abnormal adrenal physiology is the predominant factor in the patient's difficulty, and that wedge resection is not indicated. When the chief complaint is hirsutism, the authors believe there is usually little hope that wedge resection will improve the situation.

DOUGLAS M. HAYNES, M.D.

Vol. 251, No. 14, September 30, 1954.

*Ober, William B., and Reiner, Leopold: Cancer of the Cervix in Jewish Women, p. 555.
Leadbetter, Wyland F.: Cancer of the Genitourinary Tract (Concluded), p. 562.

Ober and Reiner: Cancer of the Cervix in Jewish Women, p. 555.

This report is based on the study of the records of the Beth Israel Hospital, Boston, from 1928 to 1953, on all women in whom the diagnosis of carcinoma of the cervix was verified histologically. During this period, there were 86,214 admissions, of which 76.7 per cent were Jewish. Seventy-eight of these patients had histologically proved carcinoma of the cervix. Twenty-two of these occurred in Jewish women, a rate of 33.2 per 100,000 female hospital admissions; 56 cases were found in the non-Jewish women, or a rate of 280 per 100,000. The ratio of carcinoma of the cervix in Jewish to non-Jewish women according to this study is approximately 1:9. The authors calculate from their data that if a given female population contains 5 per cent Jewish women, one in every 170 cases of cervical carcinoma will occur in a Jewish woman. With the rates per 100,000 as the basis of computation, the ratio of carcinoma of the cervix to carcinoma of the corpus uteri in Jewish women is one in four, whereas that in non-Jewish women is two in one. The incidence of carcinoma of the cervix in relation to carcinoma of the corpus of the female population of Massachusetts is approximately five to one according to the Massachusetts Department of Public Health. The authors do not believe that speculations concerning the rule of strict observance of the Talmudic prohibition of sexual intercourse for seven days after the cessation of the menses is likely to be of significance as an etiological factor; nor do they believe that it has been dogmatically established that there is a direct relationship between ritual circumcision and the infrequency of carcinoma of the cervix in Jewish women. Their study provides further evidence that carcinoma of the cervix uteri occurs much less frequently in Jewish than in non-Jewish women.

DOUGLAS M. HAYNES, M.D.

Wiener Medizinische Wochenschrift

Vol. 104, No. 28, July 10, 1954.

Czermak, H., and Krejci, A.: Prognosis in Birth Trauma, p. 555.

Vol. 104, No. 29, July 17, 1954.

Gigl, J.: Differential Diagnosis and Treatment of Tuberculosis of the Female Genital Tract, p. 577.

Vol. 104, No. 30/31, July 24, 1954.

Polmrich, A. H.: Obstetrics and Gynecology in the United States, p. 617.

Vol. 104, No. 35, August 28, 1954.

Amreich, I.: Mudpacks in Gynecology, p. 696.

Vol. 104, No. 36/37, September 4, 1954.

Zacherl, H.: The Treatment of Inoperable Carcinoma of the Genital Tract, p. 713.

Picha, E., and Weghaupt, K.: Depo-testosterone in Gynecological Carcinoma, p. 734.

Vol. 104, No. 38, September 18, 1954.

*Daniel, W.: Amputation of the Portio Vaginalis to Prevent Carcinoma of the Cervix, p. 762.

Tischer, H.: Multiple Port Radiation as Adjuvant in the Treatment of Recurrences of Carcinoma of the Female Genital Tract, p. 763.

Daniel: Amputation of the Portio Vaginalis to Prevent Carcinoma of the Cervix, p. 762.

Among 4,300 outpatients, 280 were found with cervical erosions. The highest number of erosions were found in the fourth decade of life. The correspondingly high inci-

dence of carcinoma of the cervix occurred in the fifth decade. From these facts and a review of the literature, the author comes to the conclusion that cervical erosion often leads to carcinoma of the cervix. He advocates the amputation of the cervix as a cancer prophylaxis in all cases of erosion.

WALTER F. TAUBER, M.D.

Vol. 104, No. 42, October 16, 1954.

Leb, A.: Indication, Technique and Result of Preliminary Treatment of Malignancy With X-rays, p. 835.

*Kolonja, S.. The Significance of Very Conservative Obstetrics for the Management of the Postpartum Period, p. 839.

Kolonja: Very Conservative Obstetrics and the Management of the Postpartum Period, p. 839.

It is the opinion of the author that indiscriminate use of oxytocics for stimulation of labor and for the management of the third stage, and excessive manipulation in the delivery of the baby and the placenta increase the number of complications encountered. Among 20,000 deliveries there were 630 (3.2 per cent) postpartum complications, including 432 postpartum hemorrhages, and 256 delayed separations of the placenta (over one hour). The remaining cases were variations of placenta accreta. In parallel groups of "radical" and "conservative" management, the percentage of complications breaks down to 6.7 per cent in the "radical" group and 2.5 per cent in the "conservative" group. The author, therefore, reserves stimulation of labor for true uterine inertia; postpartum oxytocics for multiple pregnancies, hydramnios, and history of previous postpartum hemorrhage. The Credé maneuver and manual removal of the placenta are used only if spontaneous delivery of the placenta has not occurred within one hour.

WALTER F. TAUBER, M.D.

Vol. 104, No. 43, October 23, 1954.

Heidler, H.: Intravenous Pituitrin in Obstetrics, p. 857.

Vol. 104, No. 44, October 30, 1954.

Leeb, H., and Rennhofer, G.: Eosin-Nigrosin Staining (Blom's Method) to Determine the Vitality of Human Sperm, p. 877.

Vol. 104, No. 46, November 13, 1954.

Schroeder, R.: Dysfunctional Bleeding, p. 907.

Vol. 104, No. 47, November 20, 1954.

Salaban, W.: Early Recognition and Treatment of Toxemia of Pregnancy, p. 931.

Kraul, L.: Indication and Results on the Conservative Treatment of Pelvic Inflammatory Disease, p. 932.

Gitsch, E.: Vaginal Cytology as an Essential Factor in the Diagnosis of the Hormonal Status in Women, p. 935.

Kohlbeck, A.: Congenital Absence of the Uterus and Hematoma of the Ovary in a Ten Year Old Girl, as Cause of Repeated Ileus, p. 936.

Correspondence

Progesterone Pregnancy Test Not New; Three Injections of Estrone a Faster Test

To the Editors:

The use of progesterone injections as a pregnancy test was discussed by Dr. Hayden in this JOURNAL, volume 69, page 931, 1955. He is under the erroneous impression that attempting to induce progesterone withdrawal bleeding as a test for pregnancy is something new, for he states that ". . . the specific application of induced withdrawal bleeding by progesterone as a diagnostic test for pregnancy has not been evaluated."

Progesterone injections have been used in Europe as a pregnancy test for ten years, the procedure being known as the Hady Gediz test. The technique for this test was first described by Dr. M. A. Hady Gediz[1] of Istanbul in 1945, and later two more papers[2, 3] on the subject were published. Hady Gediz advocated the use of five daily injections of progesterone, 10 mg. each. Reference to this test was made in a paper published in 1948 wherein was described a pregnancy test which I[4] devised, based on the use of three injections of estrone in oil.

The estrone test is applicable in all cases where progesterone can be used. The main drawback to the use of either of these hormones as a pregnancy test is that they are of no value in patients who are bleeding and they are not reliable in cases where the menstrual periods have been irregular.

The estrone pregnancy test has an advantage over progesterone in that with estrone one can set a time limit of 24 hours after the last injection for bleeding to start. If at that time there is no show of blood a diagnosis of pregnancy can be made safely in nearly all cases. In nonpregnant women a correct diagnosis often can be established within 24 hours.

The technique for the estrone pregnancy test as originally published is as follows: The test may be started at any time after the first missed menstruation. The patient is given three doses of estrone in oil, 1.0 mg. each, in the deltoid muscle over a period of five or six days. Alternate arms are used. The injections may be given on days 1-3-6, 1-4-6, or 1-4-7. The latter spacing is used in cases where under the other schedules the third dose would be given on a Sunday. If menstruation begins at any time within 24 hours after the last injection the diagnosis of nonpregnancy is made. If menstruation does not start within 24 hours after the third injection a diagnosis of pregnancy is made. About 70 per cent of the patients who are not pregnant will menstruate after only one dose of estrone. In women receiving the test, vaginal bleeding lasting less than 24 hours is not interpreted as menstruation. About 0.5 per cent of pregnant women given estrone will spot, but this does no apparent harm.

To be suitable for the estrone pregnancy test a patient should fulfill the following criteria: 1. She must have a history of reasonably regular menstrual periods. 2. Her menstrual period must be overdue. (There must be no bleeding.) 3. She must be fairly healthy in appearance with no marked anemia. 4. She must present reasonably normal findings on pelvic examination, except for signs of possible pregnancy. 5. She must have had no recent endocrine treatment other than thyroid. Except for women who are bleeding it is unusual to find a patient who is unsuitable for this test. One of the two failures

I encountered was in a patient who weighed 192 pounds and gave a false positive test. If larger doses of estrone were used in all women who weigh over 175 pounds it might be possible to eliminate these errors.

The estrone test has the highest accuracy of any pregnancy test known, closely approaching 100 per cent. It is preferable because it gives a definite diagnosis in not more than six or seven days, in contrast to the two weeks or more required for the Hady Gediz progesterone test.

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JULY 14, 1955

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2. Hady Gediz, M. A.: Turk. Arch. Gynäk. **13**: 1575, 1947.
3. Hady Gediz, M. A.: Turk Ginek. Arsivi **16**: 1827, 1951.
4. Garrett, S. S.: Am. J. Surg. **76**: 261, 1948.

Item

American Board of Obstetrics and Gynecology, Inc.

The next scheduled examination (Part I), written examination and review of case histories, for all candidates will be held in various cities of the United States, Canada, and military centers outside the continental United States, on Friday, Feb. 3, 1956.

Case abstracts numbering 20 are to be sent by the candidate to the Secretary as soon as possible after receiving notification of eligibility to the Part I written examination.

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